MOLECULAR DOCKING STUDIES OF BUTYRYL CHOLINESTERASE INHIBITORS COMPRISING ACRIDINE DERIVATIVES

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ABSTRACT

Molecular docking experiments were carried out on newly discovered acridine-derivative anti-butyrylcholinesterase inhibitors. The docking analysis showed that the suggested drugs had a weak to moderate effect on the target enzyme butyrylcholinesterase. The Protein Data Bank's accession number PDB:2XQF was utilized in docking studies. PyRx 0.9 was used to complete the docking process. Compounds 70 and 91 showed similar docking to donepezil (12.76 k/Cal), as did Compounds 40, 56, and 68 (11.1 k/Cal), Compounds 37, 48, and 72 (11.2 k/Cal), Compounds 39 and 47 (11.3 k/Cal), Compounds 38 and 67 (11.4 k/Cal), Compounds 55 and 69 (11.5 k/Cal), and Compound 69 (11.6 k/Cal). The remaining

chemicals show moderate to good activity when compared to the standard treatment. The results of ADMET prediction also revealed that these medicines would be safer and more interesting in terms of their pharmacokinetic properties.

Keywords: ADMET, Butyrylcholinesterase, Molecular Docking, PyRx

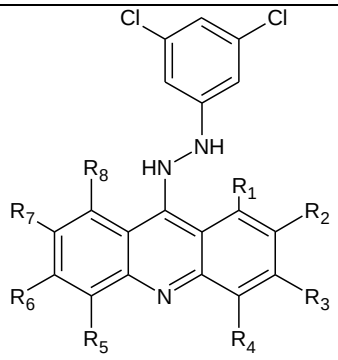
INTRODUCTION

Neurodegenerative disorders are either inherited or spontaneous causes of increasing nervous system deterioration. Alzheimer's disease (AD), Parkinson's disease (PD), and a few other less common ailments are all connected with the wasting away of central and/or peripheral nervous system tissues.The progressive deterioration in cognitive abilities and subsequent destruction of one's personality are hallmarks of Alzheimer's disease (AD), a complex and deadly neurodegenerative condition[1,2]. Cholinergic neuron loss and impaired transmission play a role in Alzheimer's disease development[3]. Anticholinesterase medications are used in the present-day management of AD to make up for the loss of the cholinergic neurotransmitter[4]. These drugs reduce the rate at which acetylcholine is broken down in the brain through a process known as cholinesterase inhibition.The increasing amount and frequency of neurotransmitter activation on postsynaptic receptors lead to improved cholinergic transmission. AChE is responsible for the hydrolysis of acetylcholine in the normal brain, whereas BChE serves a supporting function. A reduction in AChE activity and an increase in BChE activity both occur as AD progresses[5,6]. Because of this event, BChE is now an even more promising therapeutic target for ameliorating the cholinergic deficit that characterizes Alzheimer's disease[7–9]. Three cholinesterase inhibitors (rivastigmine, donepezil, and galantamine) and one NMDA receptor antagonist (memantine) are the only medications now licensed for AD[10,11]. Rivastigmine is the only cholinesterase inhibitor shown to block both acetylcholinesterase and butyrylcholinesterase.

Acridines are highly recommended scaffolds in the hunt for novel medications to treat neurological diseases[12]. Antitrypanosomal[13], Antimalarial[14], Antileishmanial, Antibacterial[15], Anticancer[16], Antiviral[17], and anti-prion medicines are only a few of the many therapeutic applications for acridine derivatives[18-20]. Anti-diabetic[21], Anti-inflammatory[22], and anti-Alzheimer properties have also been attributed to them[23-25]. Anti-TDP-43 aggregation has recently been shown to be beneficial in ALS disease models. Novel hybridization and dimeric multitarget lead and pharmaceutical possibilities may most effectively be derived from acridine derivatives.

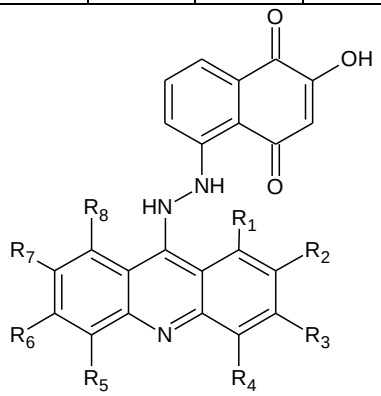
It is well-established that acridine derivatives may inhibit both acetylcholinesterase and butyrylcholinesterase[26-28]. The goal of this study is to develop novel drug-like compounds to treat AD by blocking the enzyme butyrylcholinesterase. In considering the importance of these scaffolds to the present study, we designed and evaluated a wide range of acridines. To find a potent inhibitor of the BuChE enzyme, we set out to model several potential candidates (Table 1). Subsequently, computational docking techniques were used to examine the mode of interaction between these compounds and the active site of BuChE.

Table 1: Designed Acridine Derivatives



COMPOUNDS	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
1.	H	CH_3	H	H	H	H	H	H
2.	H	H	CH_3	H	H	H	H	H
3.	H	H	H	CH_3	H	H	H	H
4.	H	OCH_3	H	H	H	H	H	H
5.	H	H	OCH_3	H	H	H	H	H
6.	H	H	H	OCH_3	H	H	H	H
7.	H	H	H	H	H	OCH_3	H	H
8.	H	H	H	H	H	H	H	H
9.	H	H	NH_2	H	H	H	H	H
10.	H	H	H	H	H	NH_2	H	H
11.	H	H	Cl	H	H	H	H	H
12.	H	H	H	Cl	H	H	H	H
13.	H	H	H	H	H	Cl	H	H
14.	H	H	H	H	H	H	Cl	H
15.	H	H	H	H	OH	H	H	H

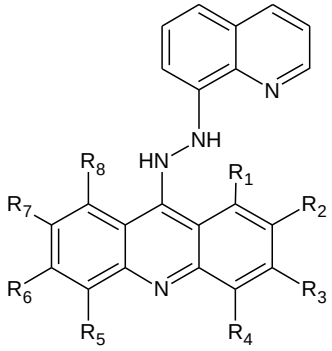
16.	H	H	H	H	H	OH	H	H
17.	H	CH_3	CH_3	H	H	H	H	H
18.	H	H	CH_3	CH_3	H	H	H	H
19.	H	CH_3	H	CH_3	H	H	H	H
20.	H	OCH_3	OCH_3	H	H	H	H	H
21.	H	H	OCH_3	OCH_3	H	H	H	H
22.	H	OCH_3	H	OCH_3	H	H	H	H
23.	H	H	H	OCH_3	H	OCH_3	H	H
24.	H	H	H	H	H	OCH_3	OCH_3	H
25.	H	OCH_3	H	H	H	H	OCH_3	H
26.	H	OCH_3	H	H	H	OCH_3	H	H
27.	H	H	OCH_3	H	H	H	OCH_3	H
28.	H	H	OCH_3	H	H	OCH_3	H	H
29.	H	H	H	OCH_3	H	OCH_3	H	H
30.	H	H	H	OCH_3	H	H	OCH_3	H
31.	H	H	Cl	Cl	H	H	H	H
32.	H	H	H	Cl	H	Cl	H	H
33.	H	H	H	H	H	Cl	Cl	H
34.	H	H	H	Cl	H	H	Cl	H
35.	H	H	NH_2	H	H	NH_2	H	H
36.	H	H	H	H	OH	OH	H	H



COMPOUNDS	**R_1**	**R_2**	**R_3**	**R_4**	**R_5**	**R_6**	**R_7**	**R_8**
37.	H	CH_3	H	H	H	H	H	H

38.	H	H	CH_3	H	H	H	H	H
39.	H	H	H	CH_3	H	H	H	H
40.	H	OCH_3	H	H	H	H	H	H
41.	H	H	OCH_3	H	H	H	H	H
42.	H	H	H	OCH_3	H	H	H	H
43.	H	H	H	H	H	OCH_3	H	H
44.	H	H	H	H	H	H	H	H
45.	H	H	NH_2	H	H	H	H	H
46.	H	H	H	H	H	NH_2	H	H
47.	H	H	Cl	H	H	H	H	H
48.	H	H	H	Cl	H	H	H	H
49.	H	H	H	H	H	Cl	H	H
50.	H	H	H	H	H	H	Cl	H
51.	H	H	H	H	OH	H	H	H
52.	H	H	H	H	H	OH	H	H
53.	H	CH_3	CH_3	H	H	H	H	H
54.	H	H	CH_3	CH_3	H	H	H	H
55.	H	CH_3	H	CH_3	H	H	H	H
56.	H	OCH_3	OCH_3	H	H	H	H	H
57.	H	H	OCH_3	OCH_3	H	H	H	H
58.	H	OCH_3	H	OCH_3	H	H	H	H
59.	H	H	H	OCH_3	H	OCH_3	H	H
60.	H	H	H	H	H	OCH_3	OCH_3	H
61.	H	OCH_3	H	H	H	H	OCH_3	H
62.	H	OCH_3	H	H	H	OCH_3	H	H
63.	H	H	OCH_3	H	H	H	OCH_3	H
64.	H	H	OCH_3	H	H	OCH_3	H	H
65.	H	H	H	OCH_3	H	OCH_3	H	H
66.	H	H	H	OCH_3	H	H	OCH_3	H
67.	H	H	Cl	Cl	H	H	H	H
68.	H	H	H	Cl	H	Cl	H	H
69.	H	H	H	H	H	Cl	Cl	H

70.	H	H	H	Cl	H	H	Cl	H
71.	H	H	NH_2	H	H	NH_2	H	H
72.	H	H	H	H	OH	OH	H	H



COMPOUNDS	**R_1**	**R_2**	**R_3**	**R_4**	**R_5**	**R_6**	**R_7**	**R_8**
73.	H	CH_3	H	H	H	H	H	H
74.	H	H	CH_3	H	H	H	H	H
75.	H	H	H	CH_3	H	H	H	H
76.	H	OCH_3	H	H	H	H	H	H
77.	H	H	OCH_3	H	H	H	H	H
78.	H	H	H	OCH_3	H	H	H	H
79.	H	H	H	H	H	OCH_3	H	H
80.	H	H	H	H	H	H	H	H
81.	H	H	NH_2	H	H	H	H	H
82.	H	H	H	H	H	NH_2	H	H
83.	H	H	Cl	H	H	H	H	H
84.	H	H	H	Cl	H	H	H	H
85.	H	H	H	H	H	Cl	H	H
86.	H	H	H	H	H	H	Cl	H
87.	H	H	H	H	OH	H	H	H
88.	H	H	H	H	H	OH	H	H
89.	H	CH_3	CH_3	H	H	H	H	H
90.	H	H	CH_3	CH_3	H	H	H	H
91.	H	CH_3	H	CH_3	H	H	H	H
92.	H	OCH_3	OCH_3	H	H	H	H	H

93.	H	H	OCH_3	OCH_3	H	H	H	H
94.	H	OCH_3	H	OCH_3	H	H	H	H
95.	H	H	H	OCH_3	H	OCH_3	H	H
96.	H	H	H	H	H	OCH_3	OCH_3	H
97.	H	OCH_3	H	H	H	H	OCH_3	H
98.	H	OCH_3	H	H	H	OCH_3	H	H
99.	H	H	OCH_3	H	H	H	OCH_3	H
100.	H	H	OCH_3	H	H	OCH_3	H	H
101.	H	H	H	OCH_3	H	OCH_3	H	H
102.	H	H	H	OCH_3	H	H	OCH_3	H
103.	H	H	Cl	Cl	H	H	H	H
104.	H	H	H	Cl	H	Cl	H	H
105.	H	H	H	H	H	Cl	Cl	H
106.	H	H	H	Cl	H	H	Cl	H
107.	H	H	NH_2	H	H	NH_2	H	H
108.	H	H	H	H	OH	OH	H	H

MATERIALS AND METHODS

Devices and materials

Docking is a technique commonly used in modern drug design to understand the relationship with the targeted ligand-receptor in addition to the desired lead chemicalcompound's connecting location with its protein receptors, and it can frequently be employed to identify connections among the target components. The study was carried out in-silico using bioinformatics technologies. We also use offline programming such as the Protein Data Bank the open website such as www.rcsb.org/pdb, draw the chemical structures using the Marvin sketch, PubChem database, andPyRx 0.9 was used for molecular docking investigations [29].

Preparation of protein

Using the protein data bank's offline program, we were able to get BuChE (PDB: 2XQF) with a resolution of 2.10. After removing the protein's crystal water, we replaced any missing hydrogens, protonated it, ionized it, and optimized its energy level. Energy

minimization was performed by using Swiss-Protein Data Bank Viewer. The Ramachandran chart is used to validate prepared protein[30].

Active site identification

Interaction profile of the ligand-protein identified https://plip-tool.biotec. plip/index.html is used to determine the presence of active amino acids in proteins. Google has an offline tool.We were able to extrapolate the protein's activated from this[31].

Ligand Preparation

The Marvin sketch tool is used to build the molecules in both two and three dimensions. After the molecule was drawn, it was optimized in 3D using Marvin sketch, and then the resulting PDB file was exported[32].

ADMET prediction in silico

Swiss ADME prediction was used to make computer predictions of the pharmacokinetic characteristics (ADMET) of potential medicines. We determined the molecule's polar surface area (PSA), the number of acceptors of hydrogen bonds (n-ON), the number of hydrogen bond donors (n-OHNH), its total central nervous system activity, its percentage of oral absorption by humans, its 1-octyl alcohol-water distribution constant (log P o/w), and its ability to cross the blood-brain barrier. Any medicine or synthetic molecule's ADME features may be better comprehended using the information offered here. Similarities between drugs, violations of the rule of five, and transgressions of the rule of three were also identified. One and only one deviation from the ideal distribution with a characteristic of 5, the molecular weight of 500, the number of H-bond donors of 5, and the number of H-bond acceptors of 10 is allowed in a given molecule [33-34].

RESULTS AND DISCUSSION

In-silico molecular docking studies

The 108 compounds for our research were created based on literature investigations of acridine derivatives, and these 108 compounds have been given to molecular docking experiments. PyRx 0.9 was used to perform molecular docking to anticipate the protein's interactions with its inhibitors. The binding mode competency of butyrylcholinesterase with 108 acridineanalogs was investigated using molecular docking. The created molecules were docked alongside the natural ligand. Good affinity for binding to a target receptor was indicated by docking values of 9 to 11 kCal/mol for our designed drugs (Table 2).

The created compounds were docked alongside the natural ligand and donepezil, a reference standard. As shown in Table 2, the docking values of our designed compounds ranged from 9.3 to 11.8kCal/mol, showing high binding affinities with the target receptor.Compounds 70 and 91 (11k/Cal), compounds 40, 56, and 68 (11.1 k/Cal), compounds 37, 48, and 72 (11.2 k/Cal), compounds 39 and 47 (11.3 k/Cal), compounds 38 and 67 (11.4 K/Cal), compounds 55 (11.5 k/Cal), and compounds 69(11.6K/Cal) shown comparable docking to donepezil (12.76 K/Cal). In comparison to normal medicine, the remaining molecule has excellent to moderate activity. Important ligand-binding domain amino acids in human BuChE inhibitors have been discovered as well. The studied ligands' major non-covalent interactions with the ligand-binding area of the BuChE inhibitors were assessed. The ligand-binding area of BuChE inhibitors, as well as certain amino acids, have been repeatedly linked to the inhibition of ligand interaction.Regular participation of these amino acids during ligand interactions with BuChE inhibitors has been demonstrated, and they also play an essential role in inhibiting of the ligand-binding region of Acetylcholinesterase inhibitors. Figures 1 to 14 depict non-covalent interactions such as hydrogen interaction, π–π - interaction, van der Waals, and Columbic interaction.

Table 2: Designed compound docking score

Ligand	Binding Affinity	Ligand	Binding Affinity	Ligand	Binding Affinity	Ligand	Binding Affinity
1	-9.8	28	-9.5	55	**-11.5**	82	-10.6
2	-9.8	29	-9.5	56	**-11.1**	83	-10.4
3	-10.1	30	-9.5	57	-10.8	84	-10.7
4	-9.5	31	-10	58	-10.5	85	-10.4
5	-9.6	32	-9.7	59	-10.9	86	-10.4
6	-9.5	33	-9.5	60	-10.9	87	-10.5
7	-9.6	34	-9.7	61	-10.2	88	-10.4
8	-9.5	35	-9.7	62	-10.8	89	-10.7
9	-10.1	36	-10.4	63	-10.9	90	-10.9
10	-10.1	37	**-11.2**	64	-10.9	91	**-11**
11	-9.7	38	**-11.4**	65	-10.9	92	-10.4

12	-9.9	39	**-11.3**	66	-10.7	93	-9.7
13	-9.7	40	**-11.1**	67	**-11.4**	94	-10.1
14	-9.6	41	-10.9	68	**-11.1**	95	-10.2
15	-10	42	-10.6	69	**-11.6**	96	-10.4
16	-10	43	-10.9	70	**-11**	97	-10
17	-9.9	44	-10.9	71	-10.7	98	-10.4
18	-10.5	45	-10.9	72	**-11.2**	99	-10.4
19	-10.1	46	-10.9	73	-10.7	100	-10.1
20	-9.5	47	**-11.3**	74	-10.5	101	-10.2
21	-9.5	48	**-11.2**	75	-10.8	102	-9.7
22	-9.4	49	**-11.3**	76	-9.9	103	-10.5
23	-9.5	50	**-11.1**	77	-10.2	104	-10.6
24	-9.7	51	**-11.3**	78	-9.9	105	-10.6
25	-9.3	52	-10.9	79	-10.2	106	-10.5
26	-9.7	53	**-11.7**	80	-9.9	107	-10.7
27	-9.6	54	**-11.8**	81	-10.6	108	-10.2

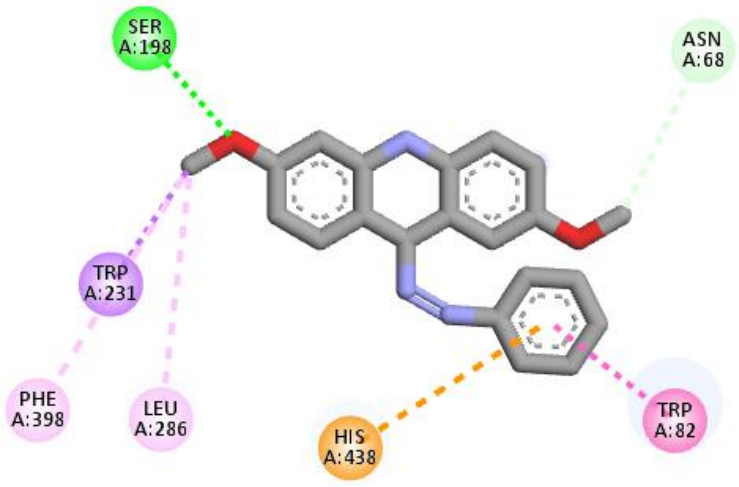


Figure 1: 2D view of interaction between the compound 37 with active site of BChE protein(2XQF)

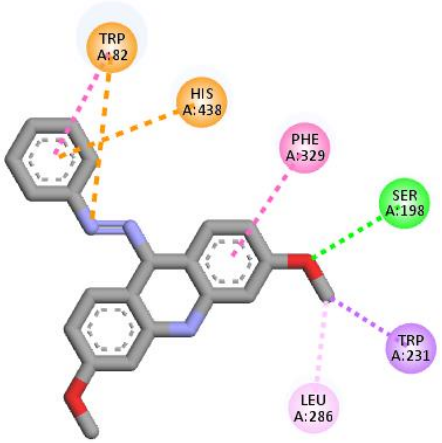


Figure 2: 2D view of interaction between the compound 38 with active site of BChE protein(2XQF)

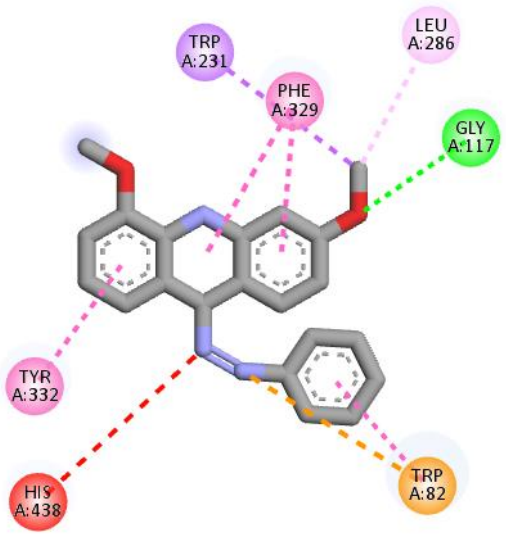


Figure 3: 2D view of interaction between the compound 39 with active site of BChE protein(2XQF)

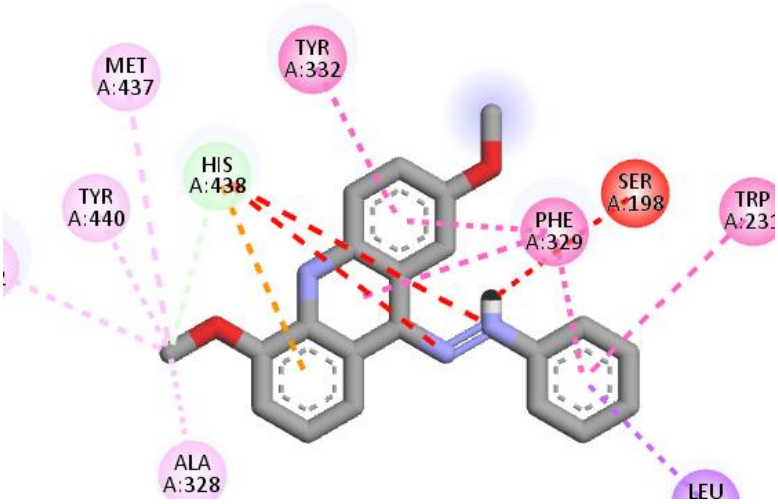


Figure 4: 2D view of interaction between the compound 40 with active site of BChE protein(2XQF)

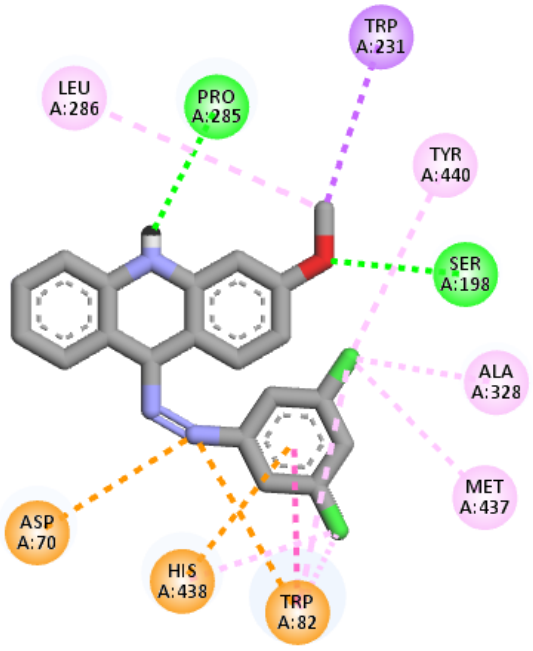


Figure 5: 2D view of interaction between the compound 47 with active site of BChE protein(2XQF)

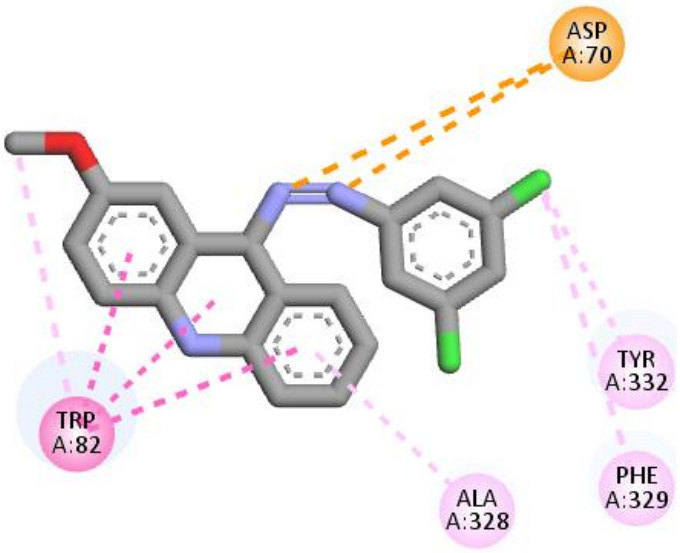


Figure 6: 2D view of interaction between the compound 48 with active site of BChE protein(2XQF)

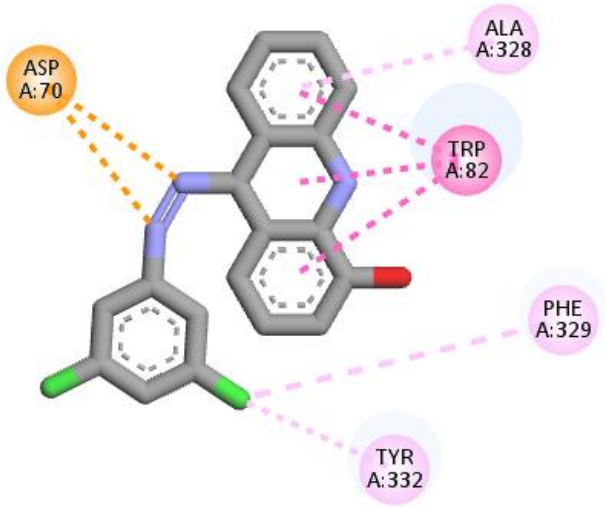


Figure 7: 2D view of interaction between the compound 55 with active site of BChE protein(2XQF)

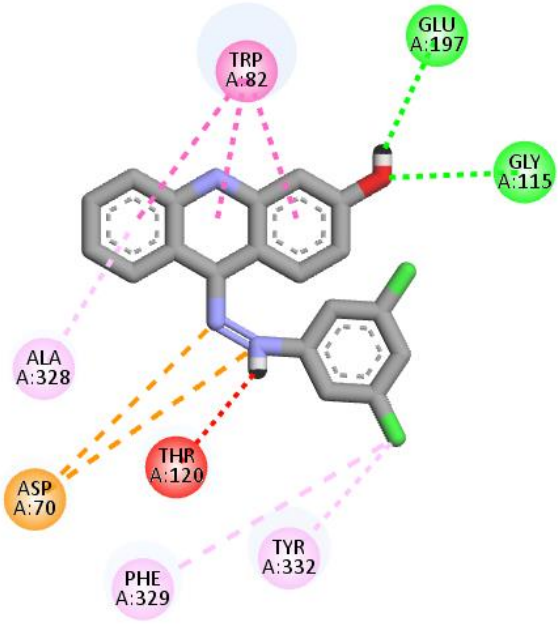


Figure 8: 2D view of interaction between the compound 56 with active site of BChE protein(2XQF)

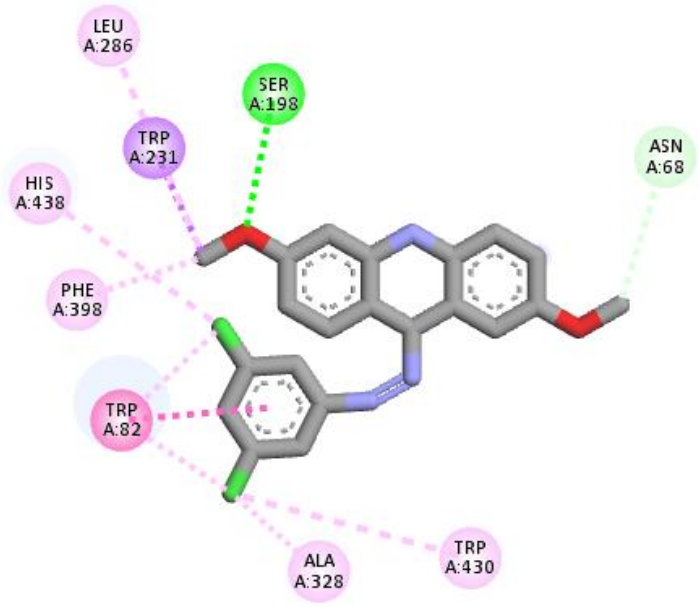


Figure 9: 2D view of interaction between the compound 67 with active site of BChE protein(2XQF)

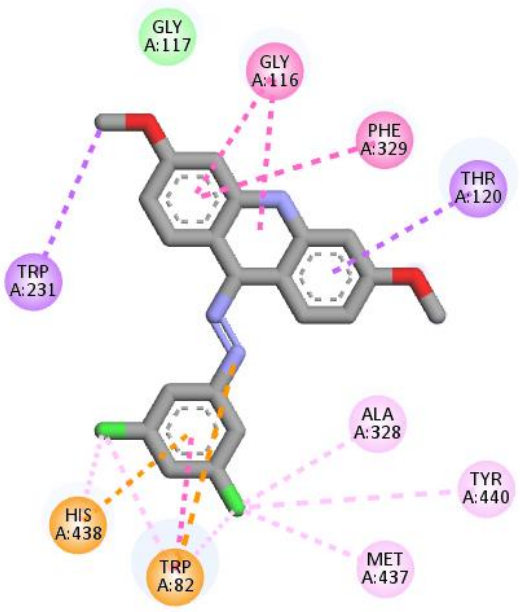


Figure 10: 2D view of interaction between the compound 68 with active site of BChE protein(2XQF)

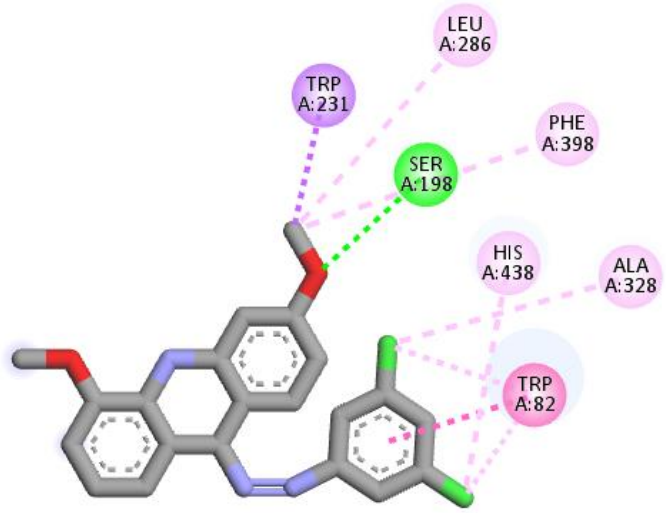


Figure 11: 2D view of interaction between the compound 69 with active site of BChE protein(2XQF)

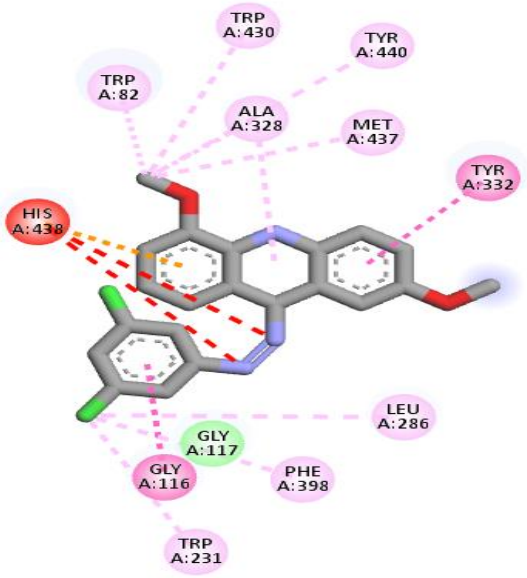


Figure 12: 2D view of interaction between the compound 70 with active site of BChE protein(2XQF)

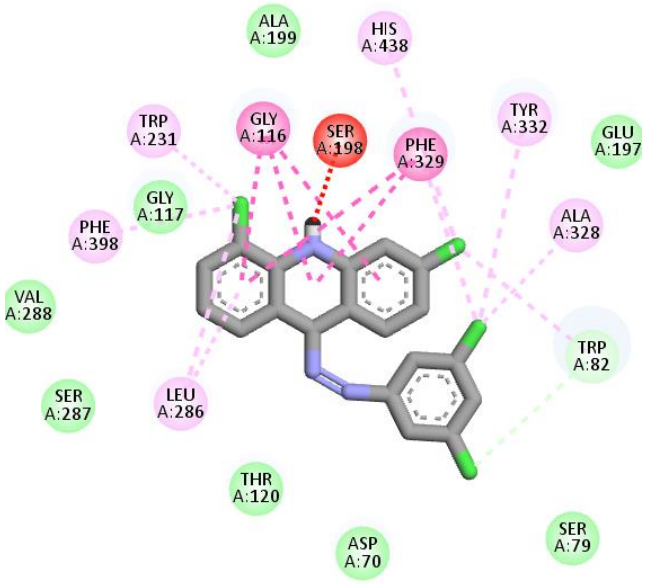


Figure 13: 2D view of interaction between the compound 72 with active site of BChE protein(2XQF)

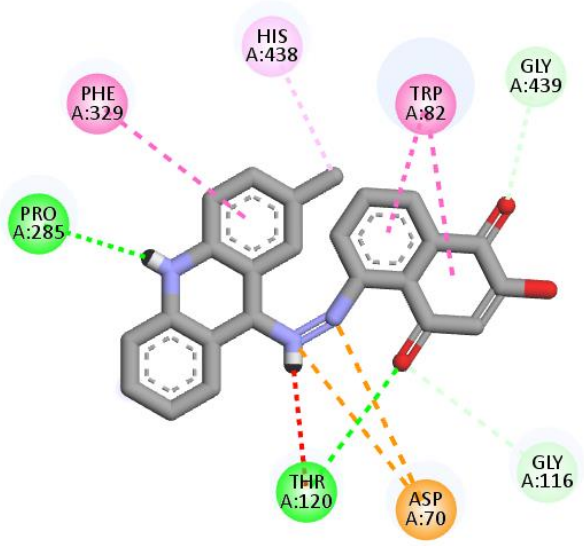


Figure 14: 2D view of interaction between the compound 91 with active site of BChE protein(2XQF)

INSILICO ADME STUDIES

SWISS ADME software was used to investigate the in-silico ADMET characteristics of the proposed ligands. The proposed compounds have molecular weights ranging from 360 to 450.The number of hydrogen bond acceptors was Calculated to be in the region of 1-6. The number of hydrogen bond donors was Calculated to be in the region of 2-4. The anticipated octanol/water partition coefficient was 2.5 to 3, and the number of plausible metabolic processes was 1-3. There were no breaches of Lipinski's rule of five. All of the substances exhibit substantial oral absorption in humans and BBB penetration. As a result, practically all of the compounds' attributes are within the suggested range. Specific in-silico ADMET characteristics of the compounds are detailed in Table 3.

Table 3. *In-silico* ADMET properties of designed compounds

Code	MW	H-bond acceptors	H-bond donors	TPSA	iLOGP	Lipinski violations	GI absorption	BBB permeant
1.	368.26	1	2	36.95	3.6	1	High	No
2.	368.26	1	2	36.95	3.6	1	High	No
3.	368.26	1	2	36.95	3.63	1	High	No
4.	384.26	2	2	46.18	3.65	1	High	Yes
5.	384.26	2	2	46.18	3.73	1	High	Yes
6.	384.26	2	2	46.18	3.55	1	High	Yes

7.	384.26	2	2	46.18	3.73	1	High	Yes
8.	384.26	2	2	46.18	3.65	1	High	Yes
9.	369.25	1	3	62.97	2.99	1	High	No
10.	369.25	1	3	62.97	2.99	1	High	No
11.	388.68	1	2	36.95	3.63	1	High	No
12.	388.68	1	2	36.95	3.53	1	High	No
13.	388.68	1	2	36.95	3.63	1	High	No
14.	388.68	1	2	36.95	3.64	1	High	No
15.	370.23	2	3	57.18	3.28	1	High	Yes
16.	370.23	2	3	57.18	3.02	1	High	Yes
17.	382.29	1	2	36.95	3.93	1	High	No
18.	382.29	1	2	36.95	3.71	1	High	No
19.	382.29	1	2	36.95	3.83	1	High	No
20.	414.28	3	2	55.41	3.84	0	High	No
21.	414.28	3	2	55.41	3.8	0	High	No
22.	414.28	3	2	55.41	3.94	0	High	No
23.	414.28	3	2	55.41	3.74	0	High	No
24.	414.28	3	2	55.41	3.84	0	High	No
25.	414.28	3	2	55.41	3.78	0	High	No
26.	414.28	3	2	55.41	3.9	0	High	No
27.	414.28	3	2	55.41	3.9	0	High	No
28.	414.28	3	2	55.41	3.99	0	High	No
29.	414.28	3	2	55.41	3.74	0	High	No
30.	414.28	3	2	55.41	3.78	0	High	No
31.	423.12	1	2	36.95	3.66	1	Low	No
32.	423.12	1	2	36.95	3.75	1	Low	No
33.	423.12	1	2	36.95	3.68	1	Low	No
34.	423.12	1	2	36.95	3.92	1	Low	No
35.	384.26	1	4	88.99	2.66	0	High	No
36.	386.23	3	4	77.41	3.21	0	High	No
37.	395.41	4	3	91.32	2.28	0	High	No
38.	395.41	4	3	91.32	2.87	0	High	No
39.	395.41	4	3	91.32	2.91	0	High	No
40.	411.41	5	3	100.55	2.82	0	High	No
41.	411.41	5	3	100.55	3.05	0	High	No
42.	411.41	5	3	100.55	2.85	0	High	No
43.	411.41	5	3	100.55	3.05	0	High	No
44.	411.41	5	3	100.55	2.82	0	High	No
45.	396.4	4	4	117.34	1.85	0	High	No
46.	396.4	4	4	117.34	1.85	0	High	No
47.	415.83	4	3	91.32	3.1	0	High	No
48.	415.83	4	3	91.32	2.89	0	High	No
49.	415.83	4	3	91.32	3.1	0	High	No
50.	415.83	4	3	91.32	3.16	0	High	No
51.	397.38	5	4	111.55	2.7	0	High	No

52.	397.38	5	4	111.55	2.41	0	High	No
53.	409.44	4	3	91.32	3.14	0	High	No
54.	409.44	4	3	91.32	3.16	0	High	No
55.	409.44	4	3	91.32	3.11	0	High	No
56.	441.44	6	3	109.78	3.12	0	High	No
57.	439.46	5	3	100.55	3.37	0	High	No
58.	441.44	6	3	109.78	3.14	0	High	No
59.	441.44	6	3	109.78	3.05	0	High	No
60.	441.44	6	3	109.78	3.06	0	High	No
61.	441.44	6	3	109.78	3.12	0	High	No
62.	441.44	6	3	109.78	3.03	0	High	No
63.	441.44	6	3	109.78	3.33	0	High	No
64.	441.44	6	3	109.78	3.18	0	High	No
65.	441.44	6	3	109.78	3.06	0	High	No
66.	441.44	6	3	109.78	3.03	0	High	No
67.	450.27	4	3	91.32	3.01	0	High	No
68.	450.27	4	3	91.32	3.16	0	High	No
69.	450.27	4	3	91.32	3.15	0	High	No
70.	450.27	4	3	91.32	3.3	0	High	No
71.	411.41	4	5	143.36	1.84	0	Low	No
72.	413.38	6	5	131.78	2.57	0	Low	No
73.	350.42	2	2	49.84	3.3	0	High	Yes
74.	350.42	2	2	49.84	3.37	0	High	Yes
75.	350.42	2	2	49.84	3.4	0	High	Yes
76.	366.42	3	2	59.07	3.42	0	High	Yes
77.	366.42	3	2	59.07	3.48	0	High	Yes
78.	366.42	3	2	59.07	3.18	0	High	Yes
79.	366.42	3	2	59.07	3.48	0	High	Yes
80.	366.42	3	2	59.07	3.42	0	High	Yes
81.	351.4	2	3	75.86	2.78	0	High	No
82.	351.4	2	3	75.86	2.78	0	High	No
83.	370.83	2	2	49.84	3.43	1	High	Yes
84.	370.83	2	2	49.84	3.21	1	High	Yes
85.	370.83	2	2	49.84	3.43	1	High	Yes
86.	370.83	2	2	49.84	3.49	1	High	Yes
87.	352.39	3	3	70.07	3.02	0	High	Yes
88.	352.39	3	3	70.07	2.85	0	High	Yes
89.	364.44	2	2	49.84	3.61	1	High	Yes
90.	364.44	2	2	49.84	3.47	1	High	Yes
91.	364.44	2	2	49.84	3.46	1	High	Yes
92.	396.44	4	2	68.3	3.53	0	High	No
93.	396.44	4	2	68.3	3.45	0	High	No
94.	396.44	4	2	68.3	3.6	0	High	No
95.	396.44	4	2	68.3	3.62	0	High	No
96.	396.44	4	2	68.3	3.53	0	High	No

97.	396.44	4	2	68.3	3.62	0	High	No
98.	396.44	4	2	68.3	3.58	0	High	No
99.	396.44	4	2	68.3	3.58	0	High	No
100.	396.44	4	2	68.3	3.62	0	High	No
101.	396.44	4	2	68.3	3.62	0	High	No
102.	396.44	4	2	68.3	3.45	0	High	No
103.	405.28	2	2	49.84	3.29	1	High	No
104.	405.28	2	2	49.84	3.58	1	High	No
105.	405.28	2	2	49.84	3.26	1	High	No
106.	405.28	2	2	49.84	3.53	1	High	No
107.	366.42	2	4	101.88	2.44	0	High	No
108.	382.41	4	4	90.3	2.72	0	High	No

CONCLUSION

Docking studies of acridine derivate molecules into the binding site of the BuChE protein molecules (PDB ID:2XQF) provided findings that were identical from those obtained with protein. Docking energy measurements showed a marginally favourable interaction with cholinesterase. According to the results of the enzyme inhibitory test, compounds 37, 38, 39, 40, 47, 48, 55, 56, 67, 68, 69, 70, 72, and 91 had protein inhibitory activity against the BuChE enzyme that was on level with that of donepezil. ADMET prediction results also revealed that these medicines will have safer pharmacokinetic and toxicological profiles. As such, the study serves as a step towards creating cutting-edge BuChE pharmaceuticals. This study suggests that further investigation is required as acridine derivatives may be evaluated as a potential candidate medicine for Alzheimer's disease.

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