Section A-Research paper

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IN SILICO EVALUATION OF ANTI CHOLINESTERASE ACTIVITY OF NOVEL ACRIDINE SCAFFOLDS

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ABSTRACT

Novel anti-butyrylcholinesterase inhibitors comprising acridine derivatives were developed and molecular docking studies were performed on these compounds. The docking study demonstrated that the proposed compounds interact with the targeted enzyme butyrylcholinesterase in a considerable to moderate manner. PDB:2XQF, which was acquired from the Protein Data Bank, was the protein used for docking investigations. Docking was accomplished using the PyRx 0.9 program. Compounds 11, 12, and 34 (11.1 k/cal), 13, 14, and 15 (11.2 k/cal), 2, 3, 31, and 36 (11.3 k/cal), 1 and 17 (11.4 K/cal), 9 and 18 (11.5 k/cal), and 10 and 16 (11.6K/cal) docked similarly to donepezil (12.76 K/cal). Among them are When compared to the reference medicine, the remaining compounds exhibit excellent to moderate activity. Furthermore, the ADMET prediction findings suggested that these drugs may be less hazardous and have more intriguing pharmacokinetic features.

Keywords: Acridine derivatives, butyrylcholinesterase, inhibitory activity, Molecular docking, SWISS ADME, pharmacokinetic study.

INTRODUCTION

Progressive nervous system failure is a characteristic of neurodegenerative illnesses, which may be spontaneous or inherited.These diseases, which are commonly characterized by atrophy of the affected central and/or peripheral nervous system tissues, include Parkinson’s disease (PD), Alzheimer's disease (AD), and other less prevalent ailments. A multifactorial, fatal neurodegenerative ailment known as Alzheimer's disease (AD) is

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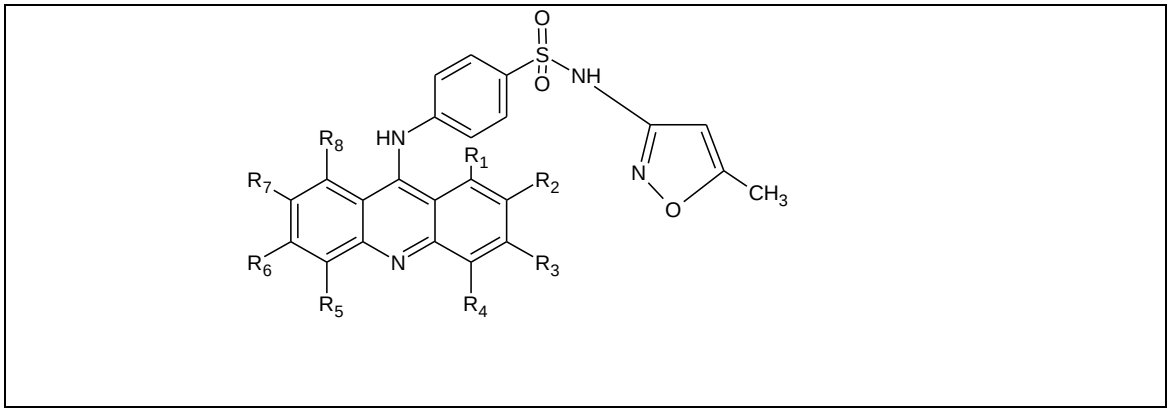
characterized by a continuous decline in cognitive ability that finally leads to complete personality impairment[1,2] Degeneration of the cholinergic neurons and reduced cholinergic transmission have a role in the aetiology of AD[3]. Anticholinesterase drugs are being used to treat AD to make up for the lack of the neurotransmitter acetylcholine[4]. These substances reduce acetylcholine hydrolysis and restore the lack of acetylcholine in the brain by blocking cholinesterases. As a consequence of the enhanced duration and strength of neurotransmitter action on postsynaptic receptors, cholinergic transmission is enhanced. AChEhydrolyzes acetylcholine principally (80%) in a healthy brain, with BChE filling in the gaps. AChE activity, on the other hand, declines as AD progresses, but BChE activity steadily increases[5, 6]. The relevance of BChE as a further therapeutic target for treating the cholinergic deficit endemic to AD is increased by this occurrence[7–9]. Only three cholinesterase inhibitors—rivastigmine, donepezil, and galantamine—as well as the NMDA receptor antagonist memantine, are currently licensed medications for the treatment of AD[10,11]. Rivastigmine is one of the cholinesterase inhibitors that has been shown to inhibit both AChE and BChE.8

In the search for new drugs to treat protozoan and neurological illnesses, acridines are regarded as favored scaffolds[10]. A wide range of therapeutic uses for acridine derivatives exists, including as antibacterial[11] antimalarial[12] antileishmanial and antitrypanosomal[13], antivirals[14], anticancer[15], and anti-prion drugs[16-18] Additionally, they have been said to have anti-inflammatory[19], anti-diabetic[20] and anti-Alzheimer effects[21-23]. In ALS illness models, they recently showed that anti-TDP-43 aggregation was effective.Acridine derivatives are the best places to start when creating new hybrid and dimeric multitarget lead and medication prospects.

The ability of members of the acridine derivatives to inhibit AChE and BChE is well documented[24-26]. This research focuses on the discovery of new drug-like molecules that inhibit the butyrylcholinesterase enzyme to treat problems associated with AD. We created and assessed a number of different acridines while keeping in mind the significance of these scaffolds in the current work. We intended to create a structure (Table 1) and investigate their BuChE enzyme inhibition in the pursuit of an efficient BuChE enzyme inhibitor. Later, the way of interaction of these compounds in the active region of BuChE was investigated using the computational docking methods.

Table 1. Designed Acridine Derivatives



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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

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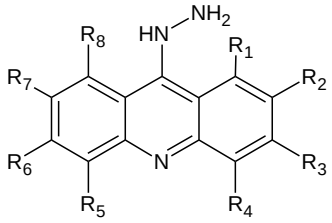

COMPOUNDS	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
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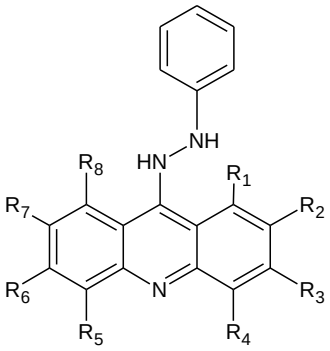
38.	H	H	CH_3	H	H	H	H	H
39.	H	H	H	CH_3	H	H	H	H
40.	H	OCH_3	H	H	H	H	H	H
41.	H	H	OCH_3	H	H	H	H	H
42.	H	H	H	OCH_3	H	H	H	H
43.	H	H	H	H	H	OCH_3	H	H
44.	H	H	H	H	H	H	H	H
45.	H	H	NH_2	H	H	H	H	H
46.	H	H	H	H	H	NH_2	H	H
47.	H	H	Cl	H	H	H	H	H
48.	H	H	H	Cl	H	H	H	H
49.	H	H	H	H	H	Cl	H	H
50.	H	H	H	H	H	H	Cl	H
51.	H	H	H	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

ISSN 2063-5346

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

ISSN 2063-5346

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 chemical compound'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, and PyRx 0.9 was used for molecular docking investigations[27].

Preparation of protein

Using the protein data bank's offline program, we were able to get BuChE (PDB: 2XQF) with a resolution of 2.10Å. 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[28].

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[29].

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[30].

ADMET prediction in silico

ISSN 2063-5346

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[31].

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 acridine analogues was investigated using molecular docking. The created molecules were docked alongside the natural ligand. Good affinity for binding to a target receptor were indicated by docking values of 7 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 7.5 to 11.6 kcal/mol, showing high binding affinities with the target receptor.Compounds 11, 12, and 34 (11.1 k/cal), compounds 13, 14, and 15 (11.2 k/cal), compounds 2, 3, 31, and 36 (11.3 k/cal), compounds 1 and 17 (11.4 K/cal), compounds 9 and 18 (11.5 k/cal), and compounds 10 and 16 (11.6K/cal) shown comparable docking to donepezil (12.76 K/cal). In comparison to the 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 16 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	**-11.4**	28	-10.2	55	-8.2	82	-9.4

ISSN 2063-5346

2	**-11.3**	29	-10	56	-8.1	83	-10.2
3	**-11.3**	30	-10.1	57	-8	84	-9.5
4	-10.7	31	**-11.3**	58	-7.9	85	-9.4
5	-10.5	32	-10.6	59	-8.1	86	-9.8
6	-10.7	33	-10.6	60	-7.2	87	-9.9
7	-10.3	34	**-11.1**	61	-7.3	88	-9.5
8	-10.4	35	-10.9	62	-7.5	89	-10.2
9	**-11.5**	36	**-11.3**	63	-7.6	90	-10.2
10	**-11.6**	37	-8.1	64	-7.9	91	-10.2
11	**-11.1**	38	-8.2	65	-8.3	92	-9.9
12	**-11.1**	39	-8.4	66	-8.4	93	-9.6
13	**-11.2**	40	-8.1	67	-8.4	94	-8.9
14	**-11.2**	41	-7.9	68	-8	95	-10.2
15	**-11.2**	42	-8.1	69	-7.8	96	-8.9
16	**-11.6**	43	-7.9	70	-8.2	97	-8.9
17	**-11.4**	44	-7.7	71	-8.6	98	-9
18	**-11.5**	45	-8.3	72	-9.8	99	-8.9
19	-10.9	46	-8.3	73	-9.7	100	-8.9
20	-10.6	47	-8	74	-9.8	101	-9.1
21	-9.9	48	-8.2	75	-9.4	102	-9.8
22	-10.4	49	-8.1	76	-9.8	103	-9.3
23	-10.2	50	-7.8	77	-10	104	-9.2
24	-10.4	51	-8.2	78	-9.1	105	-9.3
25	-10.3	52	-8.3	79	-9.4	106	-9
26	-10.4	53	-8.9	80	-9.7	107	-9.3
27	-10.4	54	-8.3	81	-9.8	108	-10.1

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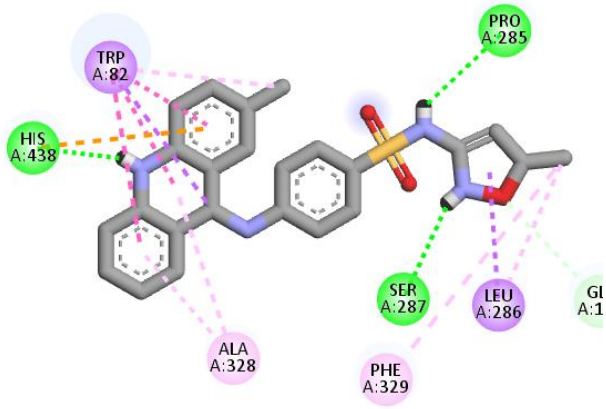

Figure 1: 2D view of interaction between the compound 1 with active site of BChE protein(2XQF)

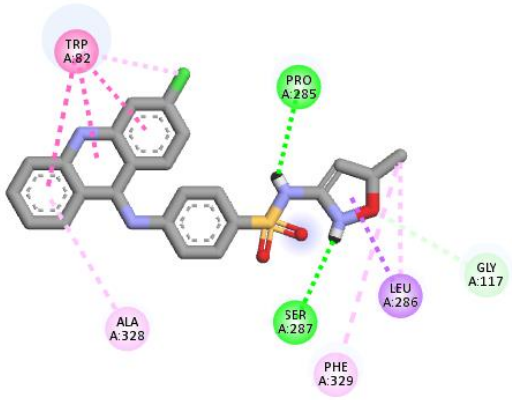

Figure 2: 2D view of interaction between the compound 2 with active site of BChEprotein(2XQF)

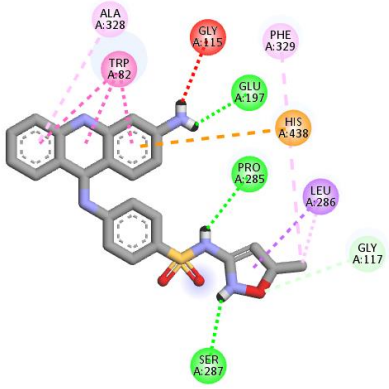

Figure 3: 2D view of interaction between the compound 3 with active site of BChE protein(2XQF)

ISSN 2063-5346

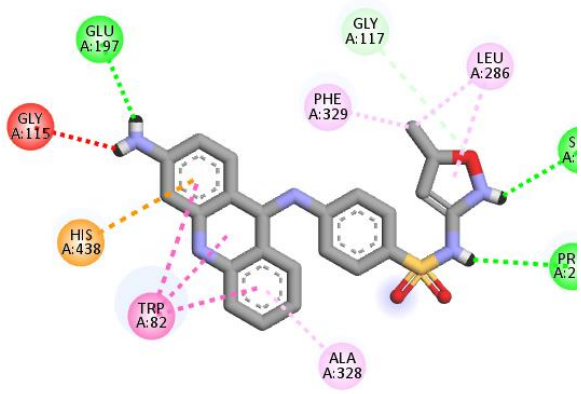

Figure 4: 2D view of interaction between the compound 9 with active site of BChE protein(2XQF)

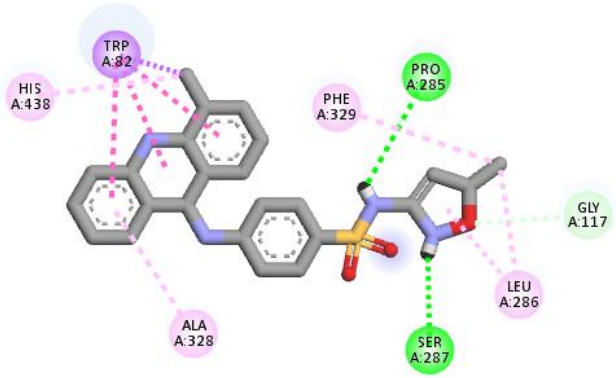

Figure 5: 2D view of interaction between the compound 10 with active site of BChE protein(2XQF)

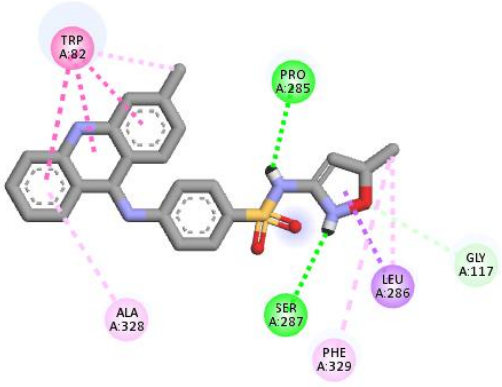

Figure 6: 2D view of interaction between the compound 11 with active site of BChE protein(2XQF)

ISSN 2063-5346

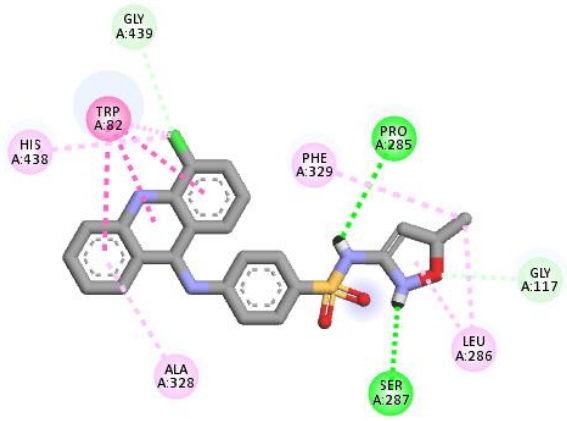

Figure 7: 2D view of interaction between the compound 12 with active site of BChE protein(2XQF)

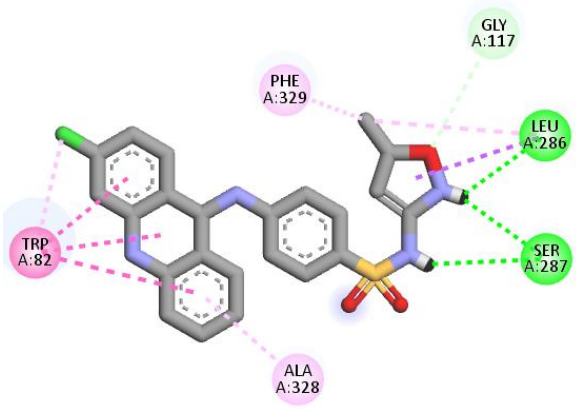

Figure 8: 2D view of interaction between the compound 13 with active site of BChE protein(2XQF)

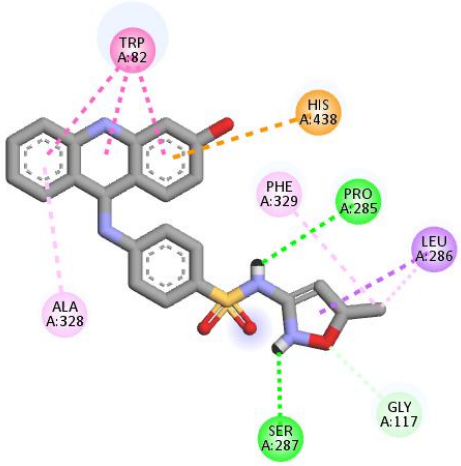

Figure 9: 2D view of interaction between the compound 14 with active site of BChE protein(2XQF)

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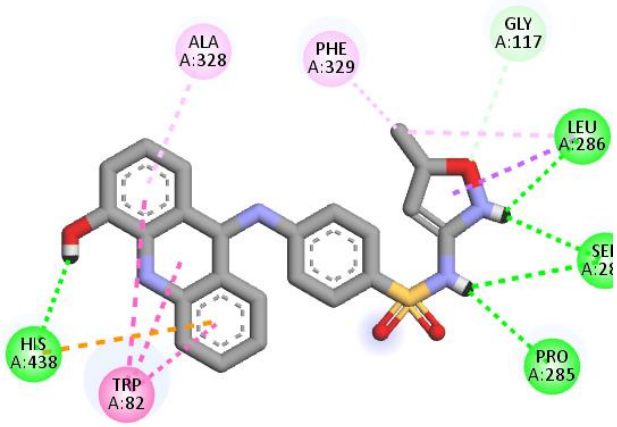

Figure 10: 2D view of interaction between the compound 15 with active site of BChE protein(2XQF)

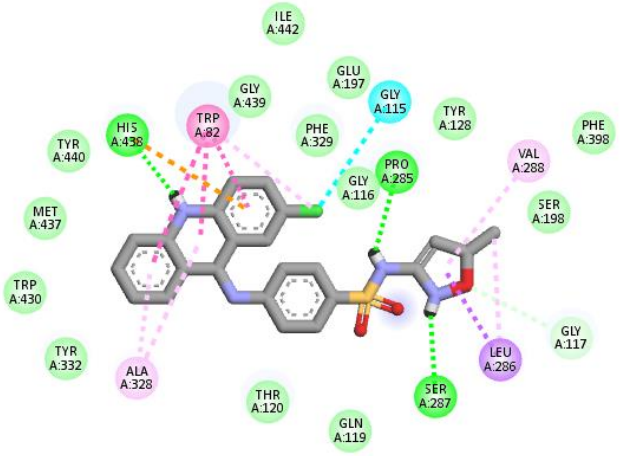

Figure 11: 2D view of interaction between the compound 16 with active site of BChE protein(2XQF)

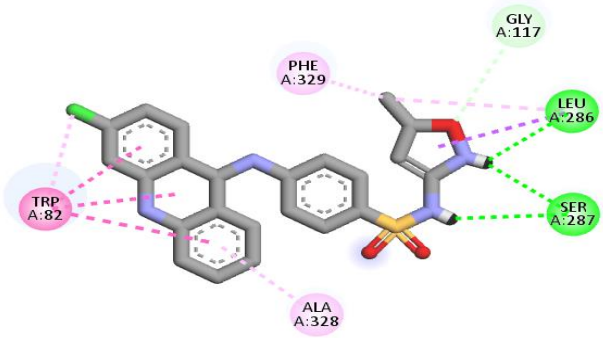

Figure 12: 2D view of interaction between the compound 17 with active site of BChE protein(2XQF)

ISSN 2063-5346

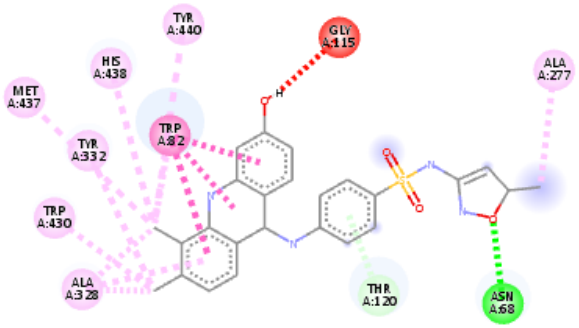

Figure 13: 2D view of interaction between the compound 18 with active site of BChE protein(2XQF)

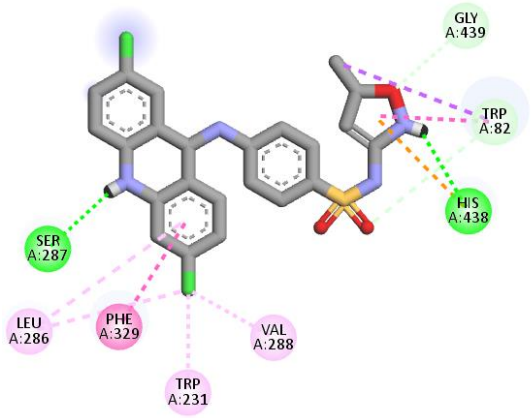

Figure 14: 2D view of interaction between the compound 31 with active site of BChE protein(2XQF)

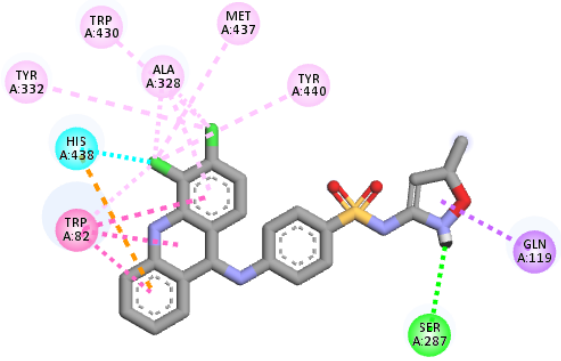

Figure 15: 2D view of interaction between the compound 32 with active site of BChE protein(2XQF)

ISSN 2063-5346

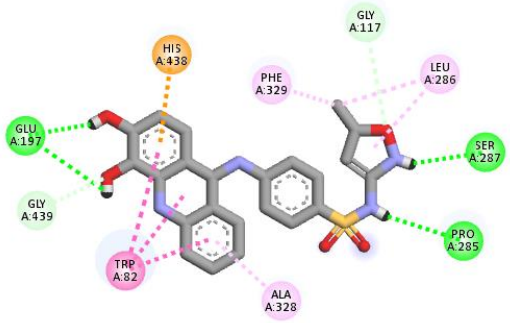

Figure 16: 2D view of interaction between the compound 33 with active site of BChE protein(2XQF)

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 230 to 480. The number of hydrogen bond donors was calculated to be in the region of 1. Four hydrogen bond acceptors were estimated. 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 desinged compounds

Code	MW	H-bond acceptors	H-bond donors	TPSA	iLOGP	Lipinski violations	GI absorption	BBB permeant
1	444.51	5	2	105.5	2.85	0	Low	No
2	444.51	5	2	105.5	3	0	Low	No
3	444.51	5	2	105.5	3.08	0	Low	No
4	460.51	6	2	114.73	2.69	0	Low	No
5	460.51	6	2	114.73	3.11	0	Low	No
6	460.51	6	2	114.73	2.96	0	Low	No
7	460.51	6	2	114.73	3.11	0	Low	No
8	460.51	6	2	114.73	2.69	0	Low	No
9	445.49	5	3	131.52	2.24	0	Low	No
10	445.49	5	3	131.52	2.24	0	Low	No
11	464.92	5	2	105.5	2.82	0	Low	No
12	464.92	5	2	105.5	2.93	0	Low	No
13	464.92	5	2	105.5	2.82	0	Low	No
14	464.92	5	2	105.5	2.73	0	Low	No
15	446.48	6	3	125.73	2.81	0	Low	No

ISSN 2063-5346

16	446.48	6	3	125.73	2.38	0	Low	No
17	474.53	6	3	125.73	3.1	0	Low	No
18	474.53	6	3	125.73	2.73	0	Low	No
19	474.53	6	3	125.73	2.75	0	Low	No
20	506.53	8	3	144.19	2.69	1	Low	No
21	506.53	8	3	144.19	2.99	1	Low	No
22	506.53	8	3	144.19	2.7	1	Low	No
23	490.53	7	2	123.96	3.17	0	Low	No
24	490.53	7	2	123.96	2.71	0	Low	No
25	490.53	7	2	123.96	3.47	0	Low	No
26	490.53	7	2	123.96	3.43	0	Low	No
27	490.53	7	2	123.96	3.43	0	Low	No
28	490.53	7	2	123.96	3.34	0	Low	No
29	490.53	7	2	123.96	3.17	0	Low	No
30	490.53	7	2	123.96	3.18	0	Low	No
31	499.37	5	2	105.5	2.84	0	Low	No
32	499.37	5	2	105.5	3.18	0	Low	No
33	499.37	5	2	105.5	2.9	0	Low	No
34	499.37	5	2	105.5	3.09	0	Low	No
35	460.51	5	4	157.54	2	0	Low	No
36	462.48	7	4	145.96	2.46	0	Low	No
37	223.27	2	2	50.94	1.98	0	High	Yes
38	239.27	3	2	60.17	2.06	0	High	Yes
39	239.27	3	2	60.17	2.21	0	High	Yes
40	239.27	3	2	60.17	1.8	0	High	Yes
41	239.27	3	2	60.17	2.21	0	High	Yes
42	243.69	2	2	50.94	2.12	0	High	Yes
43	243.69	2	2	50.94	2.18	0	High	Yes
44	243.69	2	2	50.94	2.24	0	High	Yes
45	225.25	3	3	71.17	1.84	0	High	Yes
46	225.25	3	3	71.17	1.65	0	High	Yes
47	237.3	2	2	50.94	2.19	0	High	Yes
48	237.3	2	2	50.94	2.33	0	High	Yes
49	269.3	4	2	69.4	2.19	0	High	Yes
50	269.3	4	2	69.4	2.32	0	High	Yes
51	269.3	4	2	69.4	2.43	0	High	Yes
52	269.3	4	2	69.4	2.31	0	High	Yes
53	269.3	4	2	69.4	2.19	0	High	Yes
54	269.3	4	2	69.4	2.42	0	High	Yes
55	269.3	4	2	69.4	2.5	0	High	Yes

ISSN 2063-5346

56	269.3	4	2	69.4	2.5	0	High	Yes
57	269.3	4	2	69.4	2.46	0	High	Yes
58	269.3	4	2	69.4	2.31	0	High	Yes
59	269.3	4	2	69.4	2.18	0	High	Yes
60	278.14	2	2	50.94	2.2	0	High	Yes
61	278.14	2	2	50.94	2.31	0	High	Yes
62	278.14	2	2	50.94	2.24	0	High	Yes
63	239.28	2	4	102.98	1.06	0	High	No
64	241.25	4	4	91.4	-0.34	0	High	No
65	299.37	1	2	36.95	3.2	0	High	Yes
66	299.37	1	2	36.95	3.23	0	High	Yes
67	299.37	1	2	36.95	3.23	0	High	Yes
68	315.37	2	2	46.18	3.11	0	High	Yes
69	315.37	2	2	46.18	3.27	0	High	Yes
70	315.37	2	2	46.18	3.07	0	High	Yes
71	315.37	2	2	46.18	3.27	0	High	Yes
72	315.37	2	2	46.18	3.11	0	High	Yes
73	300.36	1	3	62.97	2.61	0	High	Yes
74	300.36	1	3	62.97	2.61	0	High	Yes
75	319.79	1	2	36.95	3.23	1	High	Yes
76	319.79	1	2	36.95	3.05	1	High	Yes
77	319.79	1	2	36.95	3.23	1	High	Yes
78	319.79	1	2	36.95	3.23	1	High	Yes
79	301.34	2	3	57.18	2.97	0	High	Yes
80	301.34	2	3	57.18	2.58	0	High	Yes
81	313.4	1	2	36.95	3.4	1	High	Yes
82	313.4	1	2	36.95	3.37	1	High	Yes
83	313.4	1	2	36.95	3.34	1	High	Yes
84	345.39	3	2	55.41	3.37	0	High	Yes
85	345.39	3	2	55.41	3.37	0	High	Yes
86	345.39	3	2	55.41	3.39	0	High	Yes
87	345.39	3	2	55.41	3.42	0	High	Yes
88	345.39	3	2	55.41	3.37	0	High	Yes
89	345.39	3	2	55.41	3.54	0	High	Yes
90	345.39	3	2	55.41	3.52	0	High	Yes
91	345.39	3	2	55.41	3.52	0	High	Yes
92	345.39	3	2	55.41	3.55	0	High	Yes
93	345.39	3	2	55.41	3.42	0	High	Yes
94	345.39	3	2	55.41	3.17	0	High	Yes
95	354.23	1	2	36.95	3.36	1	High	Yes

ISSN 2063-5346

96	354.23	1	2	36.95	3.36	1	High	Yes
97	354.23	1	2	36.95	3.37	1	High	Yes
98	354.23	1	2	36.95	3.48	1	High	Yes
99	315.37	1	4	88.99	2.24	0	High	No
100	317.34	3	4	77.41	2.86	0	High	Yes
101	368.26	1	2	36.95	3.6	1	High	No
102	368.26	1	2	36.95	3.6	1	High	No
103	368.26	1	2	36.95	3.63	1	High	No
104	384.26	2	2	46.18	3.65	1	High	Yes
105	384.26	2	2	46.18	3.73	1	High	Yes
106	384.26	2	2	46.18	3.55	1	High	Yes
107	384.26	2	2	46.18	3.73	1	High	Yes
108	384.26	2	2	46.18	3.65	1	High	Yes

CONCLUSION

The binding site of the BuChE protein molecules (PDB ID: 2XQF) was docked with acridine derivate molecules, and the results were similar to those seen with protein. Measured docking energies indicated a positive, although limited, interaction with cholinesterase. The protein inhibitory activity of 1,2,3,9,10,11,12,13,14,15,16,17,18,31,34, and 36 against BuChE enzyme was comparable to that of donepezil, according to the enzyme inhibitory test. Furthermore, ADMET prediction findings suggested that these drugs may have lower toxicity and pharmacokinetic features. Thus, the research is an effort to advance towards the development of new BuChE medicines. Based on the findings of this study, it is possible to infer that N-(5-methyl-1,2-oxazol-3-yl) benzene-1-sulfonamide derivatives need additional research before being considered as a prospective candidate medication for Alzheimer's disease.

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