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Insilico Molecular Docking Studies Of Novel Acridine Derivative Inhibiting Acetylcholinesterase For Alzheimer's Disease Treatment

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ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative brain disorder that causes diminished memory and cognitive decline, and it affects millions of people throughout the world. In particular, acetylcholinesterase (AChE) inhibitors have been studied as a means of studying the cholinergic system, since low acetylcholine levels, T protein aggregation, oxidative stress, inflammatory processes, and abnormal beta-amyloid, are all related to AD. For the aim of ADMET experiments for cholinesterase inhibitors against Alzheimer's disease, a series of new acridine scaffolds were developed, docked, and predicted in this research. When compared to normal Donepezil, the proposed compound showed improved docking studies in the binding region of acetylcholinesterase enzyme when utilizing the Pyrex docking program. Compound 55 (12.6 Kcal/mol) was the most widely proposed new acridine derivative, and its inhibitory activity against AChE was mediated by two hydrogen bonding interactions. Pharmacokinetic and drug-like properties were predicted in vitro using Swiss ADME software. The pharmacokinetic characteristics of the synthetic compounds suggest that they may be effective cholinesterase inhibitors in the treatment of Alzheimer's disease

KEYWORDS: Alzheimer's disease, Acridine derivatives, Acetylcholinesterase, Molecular docking, Pharmacokinetic studies, Inhibitory activity.

INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative neurological condition characterized by cognitive decline and memory loss [1]. It affects an ever-increasing number of individuals. Neurodegeneration, a decline in brain function, delusions, anxiety, inaction, and despair are some of the hallmarks of Alzheimer's disease [2-4]. Due to the absence of effective therapies, a proper diagnosis of AD is crucial. Imaging techniques like as PET and MRI are often used to identify cases of AD. High-quality images with excellent soft-tissue contrast and enhanced spatial analysis may be obtained using MRI with no risks to the patient [2]. In contrast to positron emission tomography (PET), which uses radiotracers to detect and track alteration in neurotransmitters, metabolism rate, flow of blood in BBB, etc.[5],

Uncertainty over the cause of Alzheimer's disease may explain why there is no effective treatment available. Based on the defining aspects of Alzheimer's disease, such as the existence of extracellular amyloid-beta (A) plaques and tangles of neurofibrillary cells in the interior of cells, in addition to gliosis, the degeneration of synapses, and inflammation, many theories have been proposed to explain the illness [6-9]. The causes of Alzheimer's disease have been the subject of several theories. The A-amyloid hypothesis, the A-amyloid oligomer hypothesis, the tau hypothesis, the Ca2+ regulation theory, the presenilin is hypothesis, and the lysosome hypothesis are all examples of such theories.

Overproduction of A -amyloid peptide is thought to cause synaptotoxicity, neurotoxicity, and neurodegeneration in the form of amyloid plaques [10]. aberrant neurofibrillary structures are thought to occur due to aberrant phosphorylation of tau (tubulin-associated unit), as proposed by the tau hypothesis. In healthy cells, tau proteins connect to microtubules, increasing their stability and encouraging their polymerization [11]. These receptors belong to the G type protein-coupled receptor (GPCR) family C, the calcium-sensing receptor (CaSR) mediates calcium homeostasis and regulates intracellular signaling [12], providing support for the Ca2+ dysregulation hypothesis.

Inflammation and neurodegenerative diseases including Alzheimer's have been linked to CaSR dysregulation [13,14]. Genetic variations in genes producing presenilins, the catalytic component of -secretase, have been linked to an increased risk of developing Alzheimer's disease (AD) [15]. Presenilins are responsible for cleaving the amyloid precursor protein (APP). Finally, a lysosome hypothesis postulates that defects in the autophagy-lysosomal pathway are caused by mutations in genes controlling lysosomal pH [16].

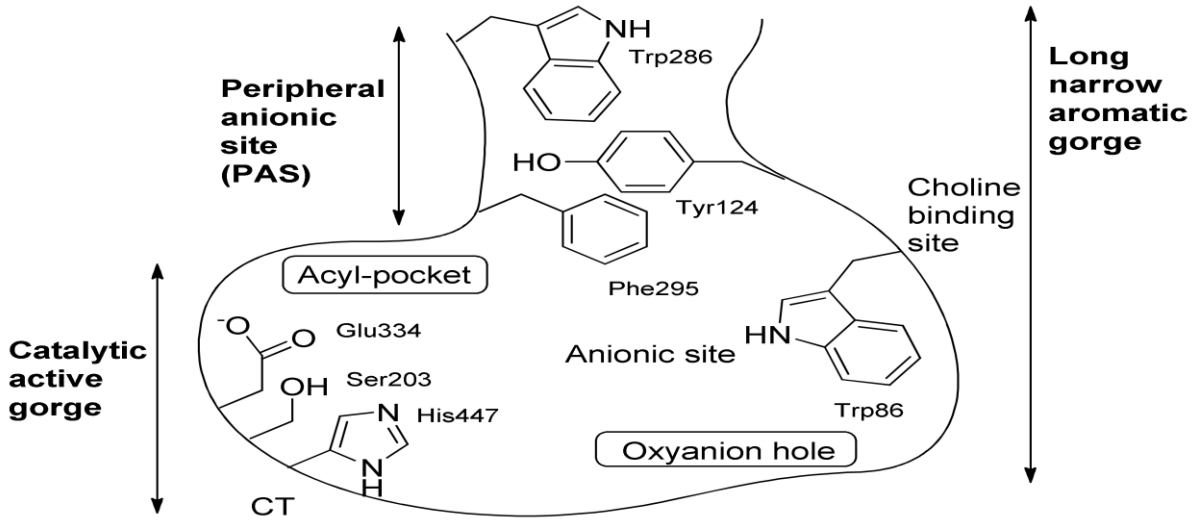
Mainly two enzymes are linked to AD namely called butyrylcholinesterase enzyme (BChE) and Acetylcholinesterase enzyme (AChE). They have been shown to increase neurotoxicity by speeding up the assembly of A peptides into Alzheimer's disease-like aggregates [17]. In AD patients, Low acetylcholine levels, aberrant -amyloid levels, T aggregation of proteins, inflammatory processes, and oxidative damage [18]. The cholinergic system, namely acetylcholinesterase (AChE) inhibitors, is now the main focus of Alzheimer's disease research.

Acetylcholinesterase (AChE) is a type-B carboxylesterase enzyme. Carboxylesterase type B refers to a group of proteins that have common ancestry [19]. Neurotransmitters acetylcholine and other choline esters are broken down by this serine hydrolase [20]. Acetylcholinesterase (AChE) is an enzyme produced by many cell types, including skeletal muscle, neurons, and hematopoietic cells, and is notable for its high catalytic efficiency. The catalytic triad of acetylcholinesterase consists of three amino acids (Glu334, His447, and Ser203) and is located at an active site that is 20 angstroms deep. Beyond Tyr337, a neighboring binding location may be found on the periphery.

Both of these locations are accessible to AChE inhibitors [21]. Studies of AChE's kinetics have shown that it has two distinct active sites, an ecstatic site for the catalytic machinery and an anionic site for the choline-active binding region [22]. The ecstatic site, degrade to choline and acetate contains a trioenzyme such as His447, Ser203 and Glu334. histidine and Serine are found in other proteases that contain serine, while aspartate is always found in the third position. Furthermore, the chirality of AChE's catalytic triad is inverted with respect to that of other proteases [23]. The acyl-enzyme is attacked by a nucleophilic water molecule, with help from the histidine, to release the choline and the acyl-enzyme. The acetic acid and the independent enzyme are produced as a consequence of this reaction [24].

Acetylcholine's positive quaternary amine, along with other cation substrates and inhibitors, participate in the c process at the anionic site. The anionic site, which scientists discovered has aromatic chemicals at the active site, is lipophilic and apolar [22].

Scheme 1 illustrating the components of the active site shared by a large number of human AChE isoforms: the acyl binding pocket; the omega loop; the oxyanion hole; the middle of the aromatic region; Ser203, Glu334, and His447, also known as the catalytic triad (CT); the anionic subsite (AS) consisting of Gly448, Glu202, Ile451, Tyr133, and Trp86 [25-27]. Reversible, pseudo-irreversible, and irreversible acetylcholinesterase inhibitors are distinguished by their respective mechanisms of action [28].

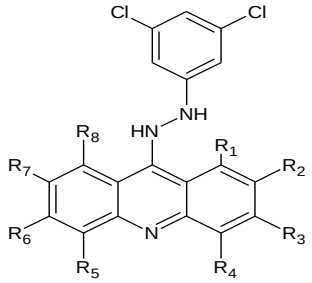


Scheme 1. Illustration of the ligand-AChE interaction.

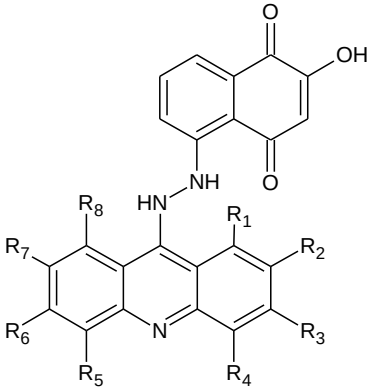
New therapeutic scaffolds based on acridines are highly sought after in the fight against protozoan and neurological diseases [29]. Some of the various therapeutic uses for acridine derivatives [30-37] include antimalarial, antitrypanosomal, antiviral, antibacterial, cancer prevention, antileishmanial, and anti-prion medications. It has also been suggested that they have anti-inflammatory, anti-Alzheimer's, and anti-diabetic characteristics [38-42]. Recently, it has been discovered that anti-TDP-43 aggregation is helpful in ALS disease models. Acridine derivatives may be the most promising source of novel multitarget lead and therapeutic candidates, including hybrid and dimeric forms.

Inhibition of acetylcholine dehydrogenase and acetylcholinesterase by acridine derivatives has been extensively documented [43-45]. Previously we study the binding site of the BuChE protein molecules docked with novel acridine and oxadiazole derivates molecules [46-49]. New drug-like compounds that block the acetylcholinesterase enzyme are the subject of this study, which aims to find effective treatments for Alzheimer's disease. We created and analyzed a variety of acridines for this investigation, bearing in mind the significance of these scaffolds. To this end, we set out to simulate a number of possible inhibitors of the AChE enzyme. Then, the nature of the interaction between these compounds and the AChE active site was investigated by in silico molecular dock techniques.

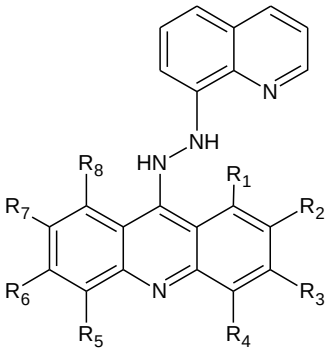
NOVEL ACRIDINE DERIVATIVATIVES



C1: R_2= CH_3	C10: **R_6**= NH_2	C19: R_2, R_4= CH_3	C28: R_3, R_6= OCH_3
C2: R_3= CH_3	C11:R_7= **R_3**= Cl	C20: R_2, R_3= OCH_3	C29: R_4, R_6= OCH_3
C3: **R_4**= CH_3	C12: **R_4**= Cl	C21: R_3, **R_4**= OCH_3	C30: R_4, R_7= OCH_3
C4: R_2=OCH_3	C13: **R_6**= Cl	C22: R_2, R_4= OCH_3	C31: R_3, **R_4**= Cl
C5: **R_3**= OCH_3	C14: R_7= Cl	C23: R_4, R_6= OCH_3	C32: R_4, R_6= Cl
C6: **R_4**= OCH_3	C15:R_5=OH	C24: R_6, R_7= OCH_3	C33: R_6, R_7= Cl
C7: **R_6**= OCH_3	C16: **R_6**= OH	C25: R_2, R_7= OCH_3	C34: R_4, R_7= Cl
C8: R_2-R_7=H	C17: R_2, R_3= CH_3	C26: R_2, R_6= OCH_3	C35: R_3, **R_6**= NH_2
C9: R_3= NH_2	C18: R_3, **R_4**= CH_3	C27: R_3, R_7= OCH_3	C36: R_5, **R_6**= OH



C37: R_2= CH_3	C46: **R_6**= NH_2	C55: R_2, R_4= CH_3	C64: R_3, R_6= OCH_3
C38: R_3= CH_3	C47:R_7= **R_3**= Cl	C56: R_2, R_3= OCH_3	C65: R_4, R_6= OCH_3
C39: **R_4**= CH_3	C48: **R_4**= Cl	C57: R_3, **R_4**= OCH_3	C66: R_4, R_7= OCH_3
C40: R_2=OCH_3	C49: **R_6**= Cl	C58: R_2, R_4= OCH_3	C67: R_3, **R_4**= Cl
C41: **R_3**= OCH_3	C50: R_7= Cl	C56: R_4, R_6= OCH_3	C68: R_4, R_6= Cl
C42: **R_4**= OCH_3	C51:R_5=OH	C60: R_6, R_7= OCH_3	C69: R_6, R_7= Cl
C43: **R_6**= OCH_3	C52: **R_6**= OH	C61: R_2, R_7= OCH_3	C70: R_4, R_7= Cl
C44: R_2-R_7=H	C53: R_2, R_3= CH_3	C62: R_2, R_6= OCH_3	C71: R_3, **R_6**= NH_2
C45: R_3= NH_2	C54: R_3, **R_4**= CH_3	C63: R_3, R_7= OCH_3	C72: R_5, **R_6**= OH



C73: R_2= CH_3	C82: **R_6**= NH_2	C91: R_2, R_4= CH_3	C100: R_3, R_6= OCH_3
C74: R_3= CH_3	C83:R_7= **R_3**= Cl	C92: R_2, R_3= OCH_3	C101: R_4, R_6= OCH_3
C75: **R_4**= CH_3	C84: **R_4**= Cl	C93: R_3, **R_4**= OCH_3	C102: R_4, R_7= OCH_3
C76: R_2=OCH_3	C85: **R_6**= Cl	C94: R_2, R_4= OCH_3	C103: R_3, **R_4**= Cl
C77: **R_3**= OCH_3	C86: R_7= Cl	C95: R_4, R_6= OCH_3	C104: R_4, R_6= Cl
C78: **R_4**= OCH_3	C87:R_5=OH	C96: R_6, R_7= OCH_3	C105: R_6, R_7= Cl
C79: **R_6**= OCH_3	C88: **R_6**= OH	C97: R_2, R_7= OCH_3	C106: R_4, R_7= Cl
C80: R_2-R_7=H	C89: R_2, R_3= CH_3	C98: R_2, R_6= OCH_3	C107: R_3, **R_6**= NH_2
C81: R_3= NH_2	C90: R_3, **R_4**= CH_3	C99: R_3, R_7= OCH_3	C108: R_5, **R_6**= OH

Methods

Nowadays, molecular dock studies is a common method used in drug discovery to learn more about how a potential lead compound would interact with a certain ligand receptor on a protein target. Using bioinformatics tools, the research was conducted virtually. In addition to databases like PubChem and molecular docking software like PyRx 0.9 available online, we also make use of offline programmes like Protein Data Bank (available at public domain websites like www.rcsb.org/pdb) and Marvin sketch for drawing chemical structures [50].

Preparation of protein

We obtained AChE (PDB: 4EY6) with a resolution of 2.40 Å using the offline program at the protein data bank. Following crystallization, we optimized the protein's energy by adding missing hydrogens, protonating it, ionizing it, and optimizing its charge. The Swiss-Protein Data Bank Viewer was used to optimize the energy budget. Protein quality may be checked using the Ramachandran chart [51]

Active site identification

We used the website plip biotech to get the ligand-protein interaction profile is a method for identifying proteins that contain functional amino acids. A Google offline tool is available. We inferred the protein's activation state based on this [52].

Ligand Preparation

Using the Marvin sketching software, the molecules are built in both three and two dimensions. The process began with a drawing of the molecule, moved on to 3D optimising in Marvin sketch, and culminated in a PDB file [53].

In silico ADMET Prediction

Estimates of the pharmacokinetic properties (ADMET) of possible drugs were made using a computer program called Swiss ADME prediction. A human's ability to orally absorb a molecule may be estimated by determining its surface area that is polar (PSA), the no. of

acceptors of hydrogen bonds (n-ON), the no. of donors of hydrogen bonds (n-OHNH), the overall activity in the central nervous system, and its percentage of oral absorption, and the distribution of the constant in 1-octyl methanol in water (log P o/w), the researchers were able to conclude that the compound was able to inhibit the activity of the central nervous system. and n-ON and n-OHNH hydrogen bond acceptor and donor numbers, we were able to determine the molecule's ability to cross the blood-brain barrier. The ADME properties of any drug or synthetic molecule may be better understood with the help of the data presented here. It was also found that there were pharmacological similarities, breaches of the rule of five, and violations of the rule of three. A molecule with a specificity of five with a molecular weight of five hundred, a count of 5 H-bond donors, and a count of 10 acceptors has an optimal distribution [54].

Results and Discussion

INSILICO MOLECULAR DOCKING STUDIES

Our investigation's 108 acridine scaffold were designed after reviewing the research on acridine derivatives in the literature, and they have been used in molecular docking studies. In order to foresee the protein's potential interactions with its inhibitors, molecular docking was performed using PyRx 0.9. Molecular docking was used to examine acetylcholinesterase's binding mode competence with 108 acridine derivatives. The synthetic molecules were anchored next to the native ligand. Docking values between 8 and 12 kcal/mol for our engineered medicines suggested an acceptable affinity for interacting to a target receptor mentioned in Table 2.

The designed compounds were docked the docking energies are compared to the standard drug donepezil. Table 2 shows that our proposed compounds have significant binding energies with the target receptor, with docking values ranging from 9.3 to 12.6 kcal/mol. Binding energies of 12 kcal/mol were observed for compounds 69,91 and 103. Binding energies of 12.1 Kcal/mol were observed for compounds 47,49,67,68 and 70. Binding energies of 12.2 Kcal/mol were observed for compounds 38 and 54. Binding energies of 12.3 Kcal/mol were observed for compounds 37 and 90. Docking results for compound 55 (12.6 K/cal) are similar to those for donepezil (12.76 K/cal). . Important ligand-binding domain amino acids found in human inhibitors of AChE have also been identified. Substitutional bonds The acetylcholinesterase inhibitor's ligand-binding domain was evaluated in conjunction with the ligands. Certain amino acids in the part of acetylcholinesterase (AChE) inhibitors that bind to ligands, as well as this part as a whole, have been linked to the reduction of ligand interactions between AChE and its inhibitors. Previous studies have shown that these particular amino acids play a recurring role in engaging with AChE inhibitors during ligand interactions, hence serving a pivotal role in obstructing the ligand-binding region of Acetylcholinesterase inhibitors. Figures 1–13 illustrate many instances of non-covalent interactions. The aforementioned interactions include hydrogen bonding, π–π stacking, van der Waals forces, and electrostatic interactions.

Table 2: docking energies of designing compounds

Ligand	Binding Affinity	Ligand	Binding Affinity	Ligand	Binding Affinity	Ligand	Binding Affinity
1	-10.7	28	-9.5	55	**-12.6**	82	-11.4
2	-10.3	29	-10.2	56	-10.3	83	-11.5
3	-10.3	30	-9.9	57	-11.4	84	-11.2
4	-10.4	31	-10.5	58	-11.9	85	-11.5
5	-9.9	32	-10.4	59	-11.3	86	-11.4
6	-10.2	33	-10.5	60	-11.1	87	-11.4
7	-9.9	34	-10.7	61	-10.6	88	-11.4
8	-10.4	35	-10.5	62	-10.9	89	-11.8
9	-10.2	36	-10.8	63	-10.8	90	**-12.3**
10	-10.2	37	**-12.3**	64	-11.2	91	**-12**
11	-10.2	38	**-12.2**	65	-11.4	92	-10.9
12	-10.2	39	-11.6	66	-11.1	93	-10.5
13	-10.2	40	-11.9	67	**-12.1**	94	-11.2
14	-10.6	41	-11.7	68	**-12.1**	95	-10.9
15	-10.1	42	-11.5	69	**-12**	96	-10.9
16	-10.2	43	-11.6	70	**-12.1**	97	-10.5
17	-10.5	44	-11.6	71	-11.8	98	-10.6
18	-10.5	45	-11.9	72	-11.7	99	-10.6
19	-10.9	46	-11.9	73	-11.6	100	-10.7
20	-10	47	**-12.1**	74	-11.7	101	-11.1
21	-9.8	48	-11.4	75	-11.3	102	-10.8
22	-10.2	49	**-12.1**	76	-11	103	**-12**
23	-10.2	50	-11.9	77	-11.1	104	-11.4
24	-10.7	51	-11.7	78	-11	105	-11.6
25	-10	52	-11.8	79	-11.1	106	-11.8
26	-9.8	53	-11.4	80	-11	107	-11.4
27	-10	54	**-12.2**	81	-11.3	108	-11.2

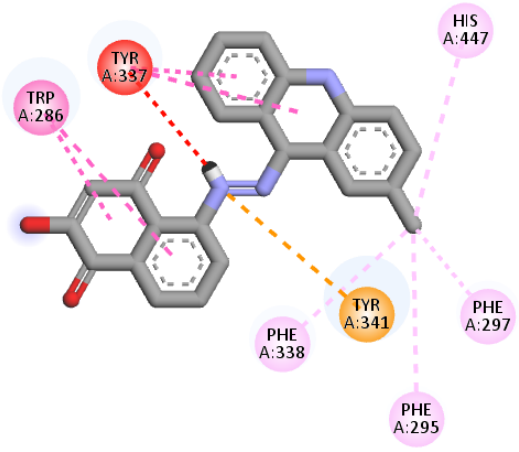


Figure 1: Compound 37 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

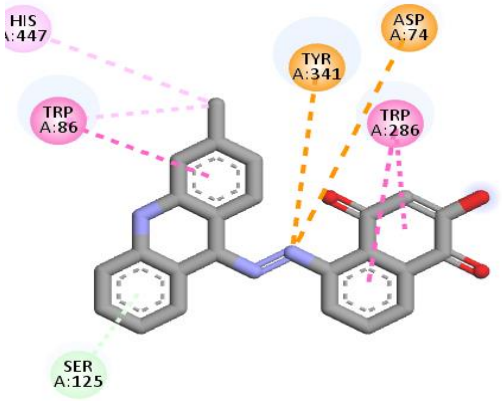


Figure 2: Compound 38 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

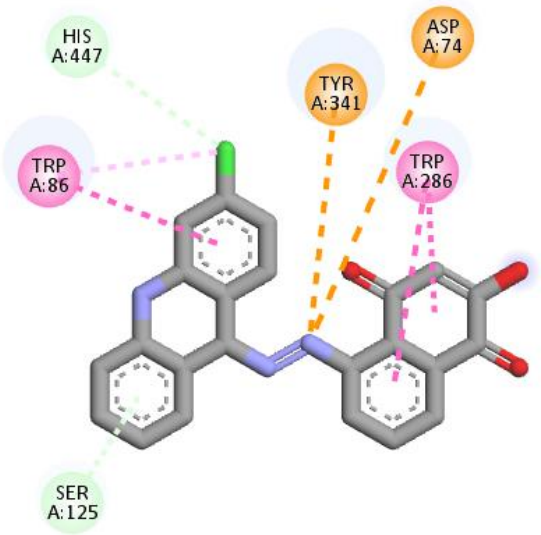


Figure 3: Compound 47 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

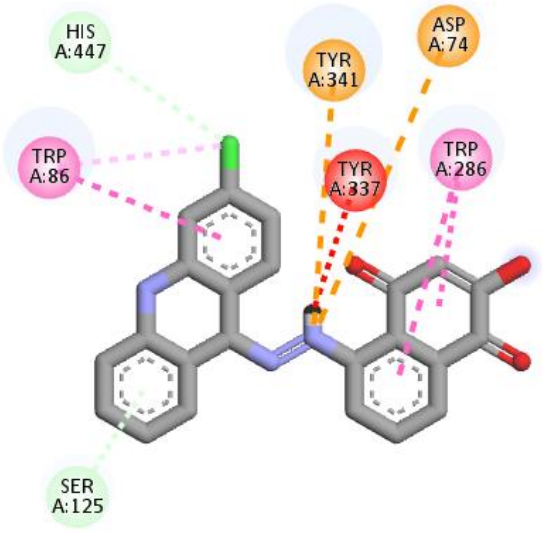


Figure 4: Compound 49 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

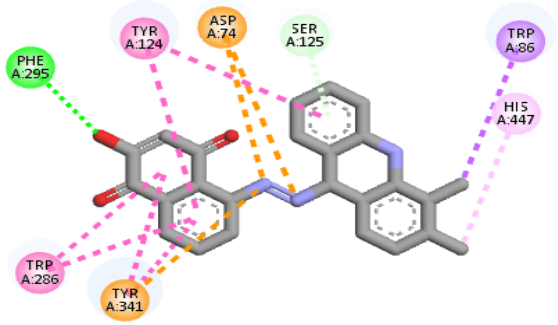


Figure 5: Compound 54 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

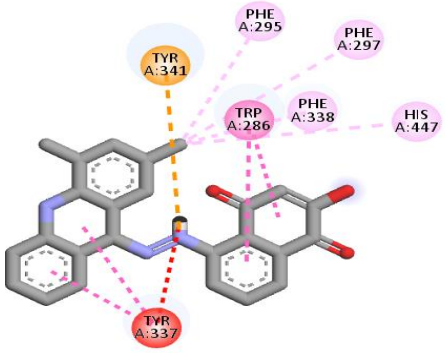


Figure 6: Compound 55 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

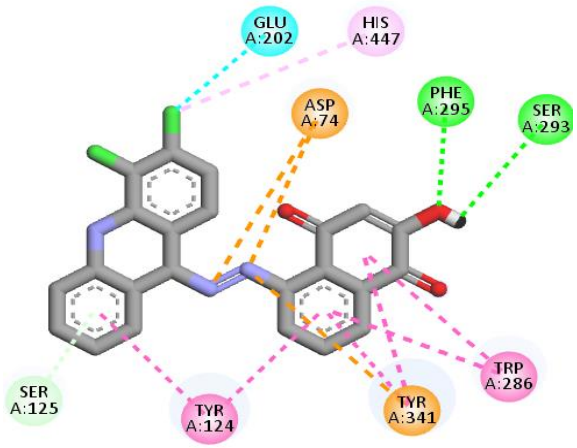


Figure 7: Compound 67 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

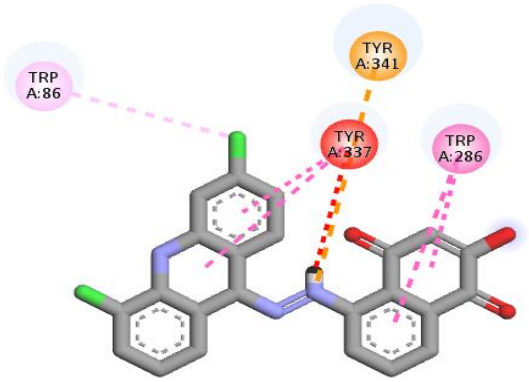


Figure 8: Compound 68 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

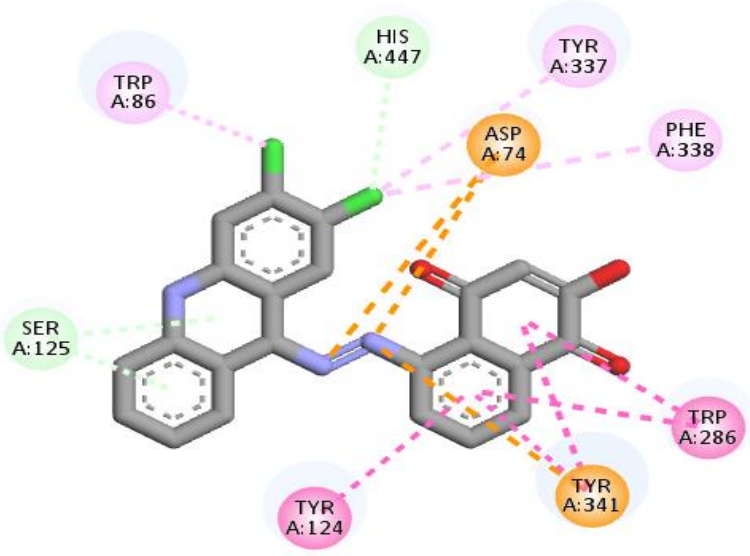


Figure 9: Compound 69 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

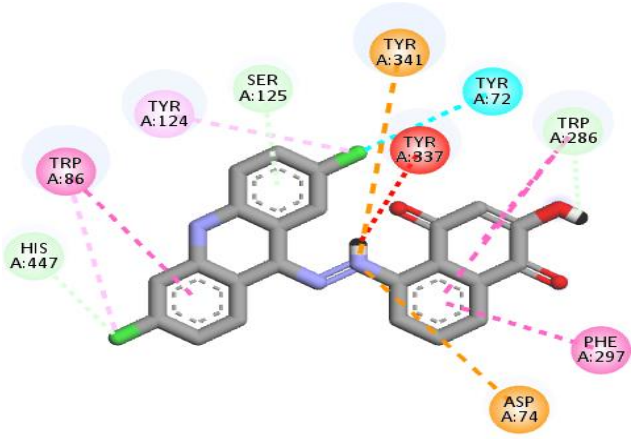


Figure 10: Compound 70 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

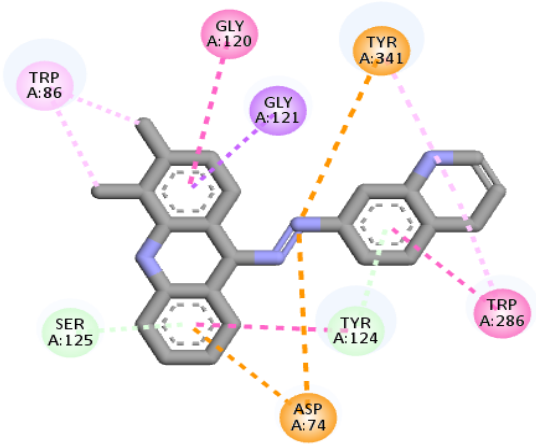


Figure 11: Compound 90 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

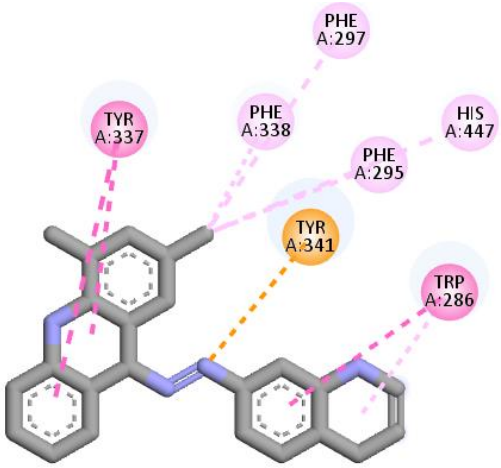


Figure 12: Compound 91 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

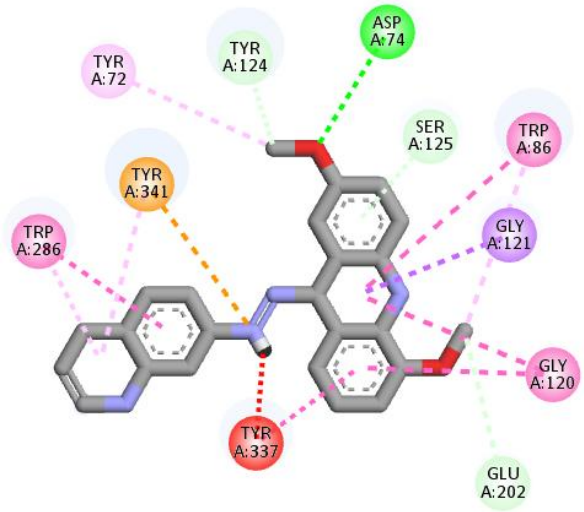


Figure 13: Compound 103 binding to the active protein region of the AChE protein (4EY6), as shown in a 2D structure.

INSILICO ADME STUDIES

The suggested ligands' The suggested ligands' in-silico ADMET properties were explored using SWISS ADME software. The molecular weights of the suggested compounds are from 230 to 480. It was determined that there was somewhere about 1 hydrogen bond donor. There were four estimated hydrogen bond acceptors. It was speculated that between one and three metabolic processes would be possible, and that the octanol/water coefficient of partition should be between 2.5 and 3. The Lipinski five-paragraph rule was not violated. All of them cross the blood-brain barrier (BBB) and are easily absorbed after being taken orally. This means that almost every property of the compounds falls within the acceptable range. Table 3 lists the compounds' individual in-silico ADMET properties.

Table 3. Designed compound ADMET characteristics in silico

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 acridine derivate molecules into the binding site of the AChE protein molecules (PDB ID:4EY6) yielded findings that were indistinguishable from those obtained with protein. Docking energy measurements suggested a weak yet favourable interaction with acetylcholinesterase Binding energies of 12.3 Kcal/mol were observed for compounds 37 and 90. Docking results for compound 55 (12.6 Kcal/ mol) are similar to those for donepezil (12.76 Kcal/mol). ADMET prediction results also revealed that these medicines will have safer pharmacokinetic and toxicological profiles. Therefore, the goal of the study is to pave the way for the creation of novel AChE drugs. The results of this study suggest that more investigation is required acridine derivatives may be evaluated as a potential candidate medicine for Alzheimer's disease.

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