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تحضير وتشخيص ودراسة الالتحام الجزيئي لمركبات ١،٣ ثيازينان -٤-اون المحضرة عن طريق تفاعل حامض ٣-مركبتوبروبانويك مع قواعد شف

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المستخلص:

في هذا العمل، تمّ تحضير أربع مركبات ذات حلقات سداسية غير متجانسة (K1-K4) باستخدام قواعد شف والكواشف المناسبة. ولتحضير قواعد شيف، تمّ تكثيف ٤-كلوروأنيلين مع ألدهيدات عطرية مختلفة في الإيثانول المطلق مع بضع قطرات من حمض الخليك الثلجي كعامل مساعد. تم الحصول على مشتق ١،٣-ثيازينان-٤-ون المعوض من مفاعلة قواعد شف المحضرة مع حامض ٣-مركابتوبروبانويك في البنزين اللامائي بالتصعيد الارتجاجي. عُزلت المنتجات ونُقيت ووُصفت باستخدام مطيافية الأشعة تحت الحمراء بتحويل فوريه ، ومطيافية الرنين النووي المغناطيسي للبروتون ومطيافية الكتلة، والتحليل الدقيق للعناصر ، استُخدمت تقنية الالتحام الجزيئي لدراسة التأثيرات المثبطة للمركبات المُنتجة (K1-K4) على نشاط أستيل كولين إستراز (AChE). أظهرت جميع مشتقات ١،٣-ثيازينان-٤-ون نشاطًا مثبطًا للإنزيم. وكشف المشتق K1، بدرجة إرساء -٩.٣ كيلو كالوري/مول، عن تأثيرات مثبطة جيدة على تثبيط AChE مقارنةً بالجالانثامين، الذي استُخدم كدواء مرجعي.

الكلمات المفتاحية: ١،٣-ثيازينان -٤-ون، إيمين، قواعد شيف، حامض ٣-مركابتوبروبانويك، الالتحام الجزيئي.

Synthesis, characterization, and molecular docking study of 1,3-thiazinan-4-one synthesized via the reaction of 3- mercaptopropanoic acid with Schiff's base

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Abstract:

Four compounds with heterocyclic six-membered rings (K1-K4) were synthesized in this work via the use of Schiff's bases and the appropriate reagents. To prepare Schiff bases, 4-chloroaniline was condensed with different aromatic aldehydes in absolute ethanol with a few drops of glacial acetic acid as a catalyst. The substituted 1,3-thiazinan-4-one was obtained by treating these Schiff bases with 3-mercaptopropanoic acid in anhydrous benzene under reflux conditions. The products were isolated, purified, and characterized by FT-IR, 1H- NMR spectroscopy, mass spectrometry, and C.H.N. analysis. Finally, molecular docking was used to investigate the inhibitory effects of the produced compounds (K1-K4) on the activity of acetylcholinesterase (AChE). All the 1,3-thiazinan-4-one derivatives showed enzyme inhibitory activity. The derivative K1, with a docking score of -9.3 kcal/mole, revealed good inhibitory effects on AChE inhibition compared with galanthamine, which was used as a reference drug.

Keywords: 1,3-Thiazinan -4-one, Imine, Schiff's Bases, 3-Mercaptopropanoic Acid, Molecular Docking.

1. INTRODUCTION

Heterocycles represent an essential molecular framework in medicinal chemistry. Many commercialized drugs contain a heterocyclic moiety that has a wide spectrum of biological activities)**Pal, 2023; Qadir, 2022).** Thiazinanes are a class of heterocycles resembling substances containing nitrogen and sulfur attached to complex structures. These types are precursors for the preparation of many drugs used to treat various diseases (**Mohamed, 2023; Kabir, 2022**). Thiazinan-4-one was first discovered in the 1960s. Since then, it has garnered a great deal of interest (**Tajdari, 2024).** The vast majority of studies focused on the structural elucidation of 1,3-thiazinan-4-one. Since the late 1990s, more studies have been conducted to develop synthetic routes (**Zhang, 2021**). With mature and stabilized synthesis, there has since been a surge in its broad application (**Alshammari, 2022; Lin, 2024).** As a versatile aggregation, thiazinan-4-one is a viable starting material for the synthesis of a variety of biologically active

compounds, and subsequent studies could promote its comprehensive application **(Ibrahim, 2023; Taylor, 2023).** Acetylcholinesterase (AChE) is an essential enzyme that hydrolyzes the neurotransmitter acetylcholine, thus maintaining homeostasis in the basal tone of the autonomic nervous system and regulating the firing of action potentials in many synapses of the central nervous system. A wide range of chemicals interacts with active AChE. **(Rajagopalan, 2023), (Xing, 2020), (Teleanu,2023).** Structure–function studies using molecular docking have shown that AChE belongs to the cholinesterase family, which also includes butyrylcholinesterase (BChE) and a wide range of bacterial enzymes (**Wojtunik-Kulesza, 2021).** Parkinsonism, myasthenia gravis, and Alzheimer's disease (AD) are neurodegenerative disorders associated with a shortage of acetylcholine due to a reduced level of the enzyme AChE (**Nimgampalle, 2023).** Furthermore, residue 199 in AChE must be glycine to catalyze the hydrolysis of acetylcholine. Molecules can bind and inhibit AChE, which is important for the treatment of neurodegenerative disorders such as AD. They can therefore be found by screening potential candidates against active site residues of the enzyme **(Permana, 2025; Halder, 2021).** The two major functional cholinesterases in humans are acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). The inhibition is recognized as a potential therapeutic target for Alzheimer's disease (AD), which is characterized by the formation of senile plaques of beta amyloid (Aβ) inside the brain (**Villeda-González, 2024).** The reduced activity of AChE and elevated levels of BChE in the brains of AD patients are implicated in aberrant cholinergic functions and the formation of senile plaques of insoluble Aβ. Currently available reversible inhibitors of cholinesterases (ChEs) do not halt the progression of the disease; hence, the rational design and development of novel compounds with a specific inhibition of BChE in the development of AD is essential. **(Chen, 2022).** Fig. 1 shows the enzyme's target proteins that need to be anticipated to foretell their inhibition.

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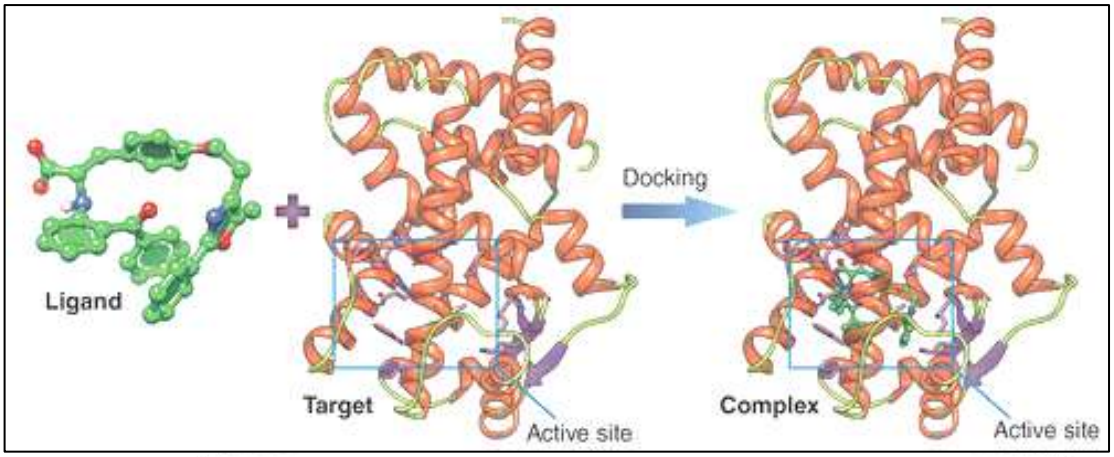

FIGURE 1. Both the ligand and the target are involved in the docking process.

2. EXPERIMENTAL SECTION

2.1. Materials and methods

For this research, the following chemicals were utilized: 4-chloroaniline, 4-bromobenzaldehyde, 4-nitrobenzaldehyde, 4-methylbenzaldehyde, 3-mercaptopropanoic acid, and Scharlau solvents. At the University of Basra, Bruker spectrometers running at 400 MHz were used to record the ^{1}H-NMR spectra. A Bruker-Tensor 27 spectrometer was used to record the FT-IR spectra using the ATR technique. The CHN lab at Iran's University of Tehran specializes in microelement analysis. An Agilent Technologies MS 5973 mass spectrometer was used to acquire the mass spectra.

2.2. General procedure for the synthesis of (4-chlorophenyl)-1-phenylmethanimine M_1-M_4

It is worth mentioning that modifications have been made on the adopted methodology Mukhlif, 2023), in which benzaldehyde (0.01 mol) was dissolved in 15 ml of absolute EtOH, and drops of glacial acetic acid were added. Then, 4-chloroaniline (0.01 mol) was dissolved in 10 ml of absolute ethanol, mixed in a 50 ml round-bottom glass flask, and left to reflux for 4 hours. The precipitate was filtered and recrystallized from EtOH.

Characterization of (E)-N-(4-chlorophenyl)-1-phenylmethanimine M1

white solid, yield 78%; m.p. 69–71 °C, FT-IR (ν cm^{-1}): 3061 (C-H$_{aromatic}$), 1624 (C=N) and 1576, 1450 (C=C).

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Characterization of (E)-1-(4-bromophenyl)-N-(4-chlorophenyl)methanimineM2

white solid, yield 79 %; m.p. 85-87 °C. FT-IR (ν cm^{-1}): 3073 ($C\text{-}H_{aromatic}$), 1622 (C=N), 1572, 1473 (C=C), and 561 (C-Br).

Characterization of (E)-N-(4-chlorophenyl)-1-(4-nitrophenyl)methanimine M3

Yellow solid, yield 82%; m.p. 108-110 °C. FT-IR (ν cm^{-1}): 3100 ($C\text{-}H_{aromatic}$), 1626 (C=N), 1590, 1413 (C=C) and 1501 ($C\text{-}NO_{2\ asy.}$) 1340 ($C\text{-}NO_{2\ sym.}$)

Characterization of (E)-N-(4-chlorophenyl)-1-(4-methoxyphenyl)methanimine M4

white solid, yield 79%; m.p. 76-78 °C. FT-IR (ν cm^{-1}): 3066 ($C\text{-}H_{\ aromatic}$), 1624 (C=N), 1509, 1440 (C=C), and 2974 ($C\text{-}H_{\ aliphatic}$).

2.3. General procedure for the synthesis of 3-(4-chlorophenyl)-2-phenyl-1,3-thiazinan-4-one K1-K4

Modifications have been made to the method used by **Adriana (2019)**. Dissolve 0.03 mol of compound M1 in 60 mL of benzene. Then (0.03 mol) of zinc chloride anhydrous dissolved in 10 ml of benzene as a catalyst was added to (0.03 mol) of 3-mercaptopropionic acid. The solutions were mixed together in a 100 ml round-bottomed glass flask. The mixture was heated for 18 h. The product was cooled, then filtered and recrystallized from absolute ethanol.

Characterization of 3-(4-chlorophenyl)-2-phenyl-1,3-thiazinan-4-one K1

Yellow solid, yield 58 %; m.p. 87–89 °C Chemical Formula ($C_{16}H_{14}ClNOS$) C.H.N. Analysis Cal./(found): C%= 63.26/(63.02), H%= 4.65/(4.31), N%= 4.61/(4.39). Mass spectrometry:- M^+ ion: $[C_{16}H_{13}ClNOS]^+$ m/z: 302.1 and base peak $[C_7H_7]^+$ m/z: 91.1. ^{1}H-NMR (DMSO-d_6, 400 MHz) δ (ppm): 7.21-7.84 (m, 9H), 6.09 (s, 1H $CH_{Thiazinan\text{-}4\text{-}one}$) and 2.68-2.98 (t, 4H $CH_{2Thiazinan\text{-}4\text{-}one}$). FT-IR ($\nu$ cm^{-1}): 3034 ($C\text{-}H_{arom.}$), 2926 ($C\text{-}H_{alip.}$), 1665 ($C{=}O_{\ lactam}$), and 717 (C-S) and 761(C-Cl).

Characterization of 2-(4-bromophenyl)-3-(4-chlorophenyl)-1,3-thiazinan-4-one K2

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Yellow solid, yield 62%; m.p. 116-118 °C. Chemical formula ($C_{16}H_{13}BrClNOS$) C.H.N. Analysis Cal./(found): C%= 50.22/(49.83), H%= 3.42/(3.02), N%= 3.66/(3.19). Mass spectrometry:- M^+ ion: $[C_{16}H_{12}BrClNOS]^+$ m/z: 379.1 and base peak $[C_7H_7]^+$ m/z: 91.1. ^{1}HNMR (DMSO-d_6, 400 MHz) δ (ppm): 7.15–7.86 (m, 8H$_{aroma.}$), 6.19 (s, 1H $CH_{Thiazinan\text{-}4\text{-}one}$) and 2.73-2.95 (t, 4H $CH_{2\ Thiazinan\text{-}4\text{-}one}$). FT-IR ($\nu$ cm^{-1}): 3034 (C-H$_{arom.}$), 2915 (C-H$_{alip.}$), 1685 (C=O $_{lactam}$), 726 (C-S), and 624 (C-Br).

Characterization of 3-(4-chlorophenyl)-2-(4-nitrophenyl)-1,3-thiazinan-4-one K3

Yellow solid, yield 69%; m.p. 119–121 °C. Chemical formula ($C_{16}H_{13}ClN_2O_3S$) C.H.N. Analysis Cal./(found): C%= 55.10/(54.76), H%= 3.76/(3.43), N%= 8.03/(7.85). Mass spectrometry:- M+ ion: $[C_{16}H_{12}ClN_2O_3S]^+$ m/z: 347.1 and base peak $[C_7H_6]^{\bullet+}$ m/z: 90.1. ^{1}HNMR (DMSO-d_6, 400 MHz) δ (ppm): 7.16-8.26 (m, 8H $_{Ar.}$), 6.23 (s, 1H $CH_{Thiazinan\text{-}4\text{-}one}$) and 2.74-2.97 (t, 4H $CH_{\ 2Thiazinan\text{-}4\text{-}one}$). FT-IR-($\nu$ cm^{-1}): 3036 (C-H$_{arom.}$), 2939 (C-H$_{alip.}$), 1636 (C=O $_{lactam}$), 739 (C-S) and 1563 (C-$NO_{2\ asy.}$) 1338 (C-$NO_{2\ sym.}$)

Characterization of 3-(4-chlorophenyl)-2-(4-methoxyphenyl)-1,3-thiazinan-4-one K4

Yellow solid, yield 62%; m.p. 93-95 °C. Chemical formula ($C_{17}H_{16}ClNO_2S$) C.H.N. Analysis Cal./(found): C%= 61.16/(60.84), H%= 4.83/(4.41), N%= 4.20/(3.84). Mass spectrometry: M+ ion: $[C_{17}H_{15}ClNO_2S]^+$ m/z: 332.1 and base peak $[C_7H_7]^+$ m/z: 91.1. ^{1}HNMR (DMSO-d_6, 400 MHz) δ (ppm): 6.96-7.98 (m, 8H$_{arom.}$), 6.16 (s, 1H $CH_{Thiazinan\text{-}4\text{-}one}$), 3.92 (s, 3H –$OCH_3$) and 2.70-2.92 (t, 4H $CH_{2Thiazinan\text{-}4\text{-}one}$). FT-IR ($\nu$ cm^{-1}): 3113 (C-H$_{arom.}$), 2988 (C-H$_{alip.}$), 1661 (C=O $_{lactam}$), and 729 (C-S).

3. THEORETICAL SECTION

3.1 In docking studies

One useful way to investigate ligand–target protein interactions is molecular docking. The effectiveness of newly synthesized heterocyclic compounds against acetylcholinesterase (AChE) (PDB-ID 1EEA) was confirmed, where an enzyme responsible for neurological diseases was

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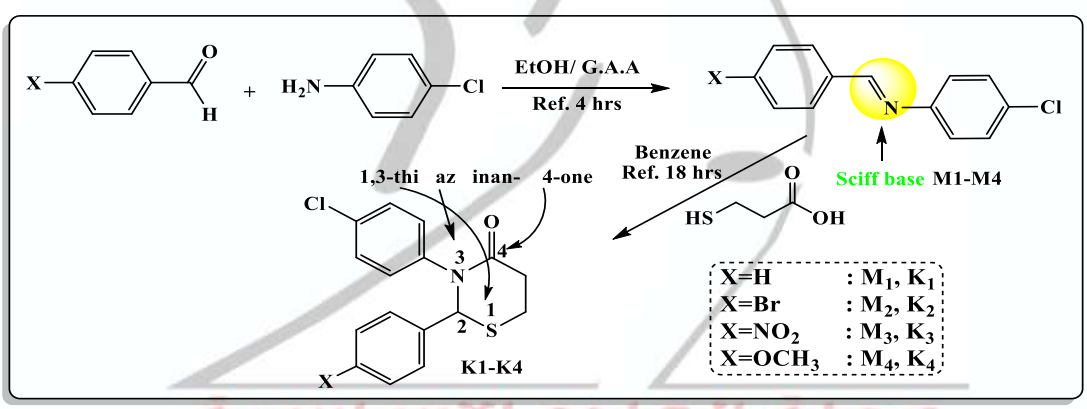
compared with that of the reference medication galanthamine (gala). Several of these enzymes can be found in the Protein Data Bank (www.pdb.org). For molecular docking, AutoDock Vina 1.5.6 was used (Trott, 2010). The compounds (K1-K5) and the reference medication were drawn using ChemDraw. The final products using Chem3D16.0 and the MMFF94 method were geometrically optimized. Afterward, BIOVIA Discovery Studio 4.0 was used to analyze the molecular docking outcomes. It was possible to identify the inhibitors that had the strongest impact on the enzyme compared to the medication by observing the ligand–protein interaction at the active site (Biovia, 2013).

4. RESULTS AND DISCUSSION

4.1. Chemistry

The routes used to synthesize compounds M1-M4 and K1-K4 are shown in Scheme 1.



Scheme 1: Steps for the synthesis of chemicals

5. Characterization

5.1. **FT-IR, ^{1}H- NMR,** C.H.N. analysis, **and mass spectrum**

Changes in the product color and melting point serve as preliminary evidence of the synthesis of imine (M_1-M_4). The FT-IR spectrum of the compounds revealed moderate absorption in the range of 3100-3061 cm^{-1} attributed to the C–H aromatic, and an absorption band in the range of 1626-1622 cm^{-1} attributed to C=N Imine was provided (Mukhlif, 2023). Table 1

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shows the absorption of each particular compound, together with the stretching absorption of the other groups.

Table 1. FT-IR spectral data (cm^{-1}) for the synthesized M_1-M_4 compounds

Code	C-H $_{Arom.}$	C=N	C=C		Others
M1	3061	1624	1576	1450	…….
M2	3073	1622	1572	1473	C-Br 561
M3	3100	1626	1590	1413	NO_2 asy. 1501 Sym. 1340
M4	3066	1624	1509	1440	C-H $_{alip.}$ 2974

The structures of the synthesized (K_1-K_4) were confirmed by FT-IR, ^{1}H-NMR, C.H.N., and mass spectra of the products. The FT-IR spectra revealed that the signature absorption bands of the (C=N) Imine group vanished. In addition to the stretching absorption of the other groups in the structure of each molecule, as shown in Table 2, both (C=O lactam) often exhibit absorption frequencies in the (1685-1661) cm^{-1} range (Mukhlif, 2025).

Table 2. FT-IR spectral data (cm-1) for synthesized K1-K4 compounds

Code	C-H		C=O lactam	C-S	Others
	Arom.	Alip.			
K1	3034	2926	1665	717	…….
K 2	3034	2915	1685	726	C-Br 624
K 3	3036	2939	1636	739	NO2 asy. 1563 Sym. 1338
K 4	3113	2988	1661	729	C-O 1010

Table 3 lists the predicted signals of each proton in various environments, and the results of the chemical shifts in the ^{1}H-NMR spectra of the product's unique molecular structures are fairly consistent with these signals. Figure 2 of compounds that have been prepared (K_1-K_4). C.H.N.% provided further proof, as the proportion of these elements that were found matches the percentages that were calculated (Adriana, 2019). Table 3 shows that the acquired analytical results correspond with reference values. For substances

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K_1-K_4, the values of the molecular ion and base peaks were visible, as shown in Table 3. The mass spectral chart for compound K1 is shown in Figure 3, and its fragmentation pattern is described in Scheme 2.

Table 3. 1H, C.H.N. Analysis and mass spectra of the K1-K4 compounds

Code	^{1}H NMR chemical shift (ppm)			C.H.N Analysis Cal./(Found.)				Mass Spectra	
	C-$H_{arom.}$	C-H Thiazinan-4-one	CH_2 Thiazinan-4-one	Chemical Formula	%C	%H	% N	Molecular Ion	Base Peak
K_1	m 9H 7.21-7.84	s 1H 6.09	t 4H 2.68-2.98	$C_{16}H_{14}ClNOS$	63.26 (63.02)	4.65 (4.31)	4.61 (4.39)	$[C_{16}H_{13}ClNOS]^+$ m/z: 302.1	$[C_7H_7]^+$ m/z: 91.1
K_2	m 8H 7.15-7.86	s 1H 6.19	t 4H 2.73-2.95	$C_{16}H_{13}BrClNOS$	50.22 (49.83)	3.42 (3.02)	3.66 (3.19)	$[C_{16}H_{12}BrClNOS]^+$ m/z: 379.1	$[C_7H_7]^{\bullet+}$ m/z: 91.1
K_3	m 8H 7.16-8.26	s 1H 6.23	t 4H 2.74-2.97	$C_{16}H_{13}ClN_2O_3S$	55.10 (54.76)	3.76 (3.43)	8.03 (7.85)	$[C_{16}H_{12}ClN_2O_3S]^+$ m/z: 347.1	$[C_7H_6]^+$ m/z: 90.1
K_4	m 8H 6.96-7.98	s 1H 6.16	t 4H 2.70-2.92	$C_{16}H_{13}BrClNOS$	50.22 (49.83)	3.42 (3.02)	3.66 (3.19)	$[C_{17}H_{15}ClNO_2S]^+$ m/z: 332.1	$[C_7H_7]^{\bullet+}$ m/z: 91.1

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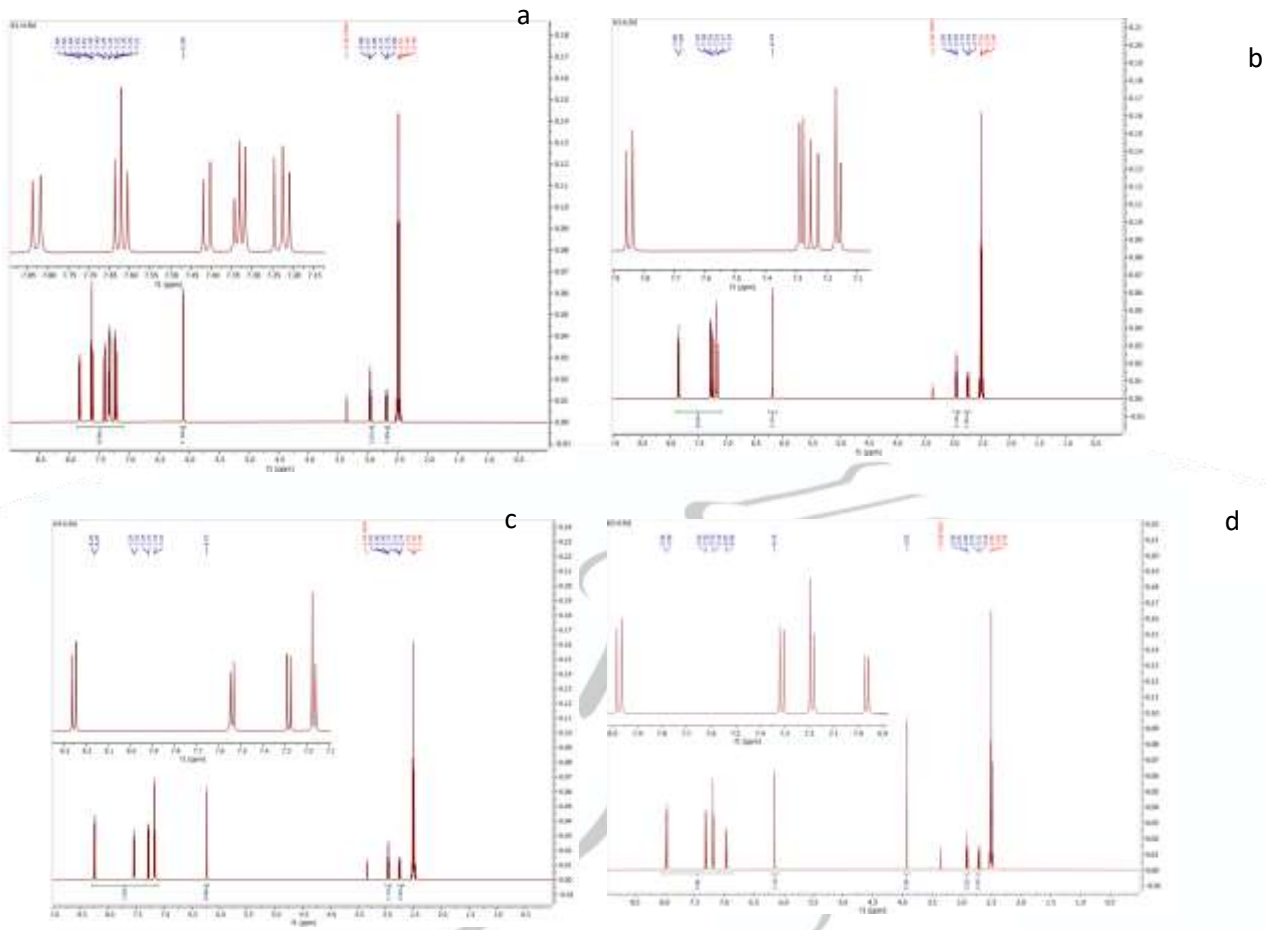

Figure 2: 1 H-NMR spectrum of compounds a) cmop. K1 b) cmop. K2 c) cmop. K3 d) cmop. K4

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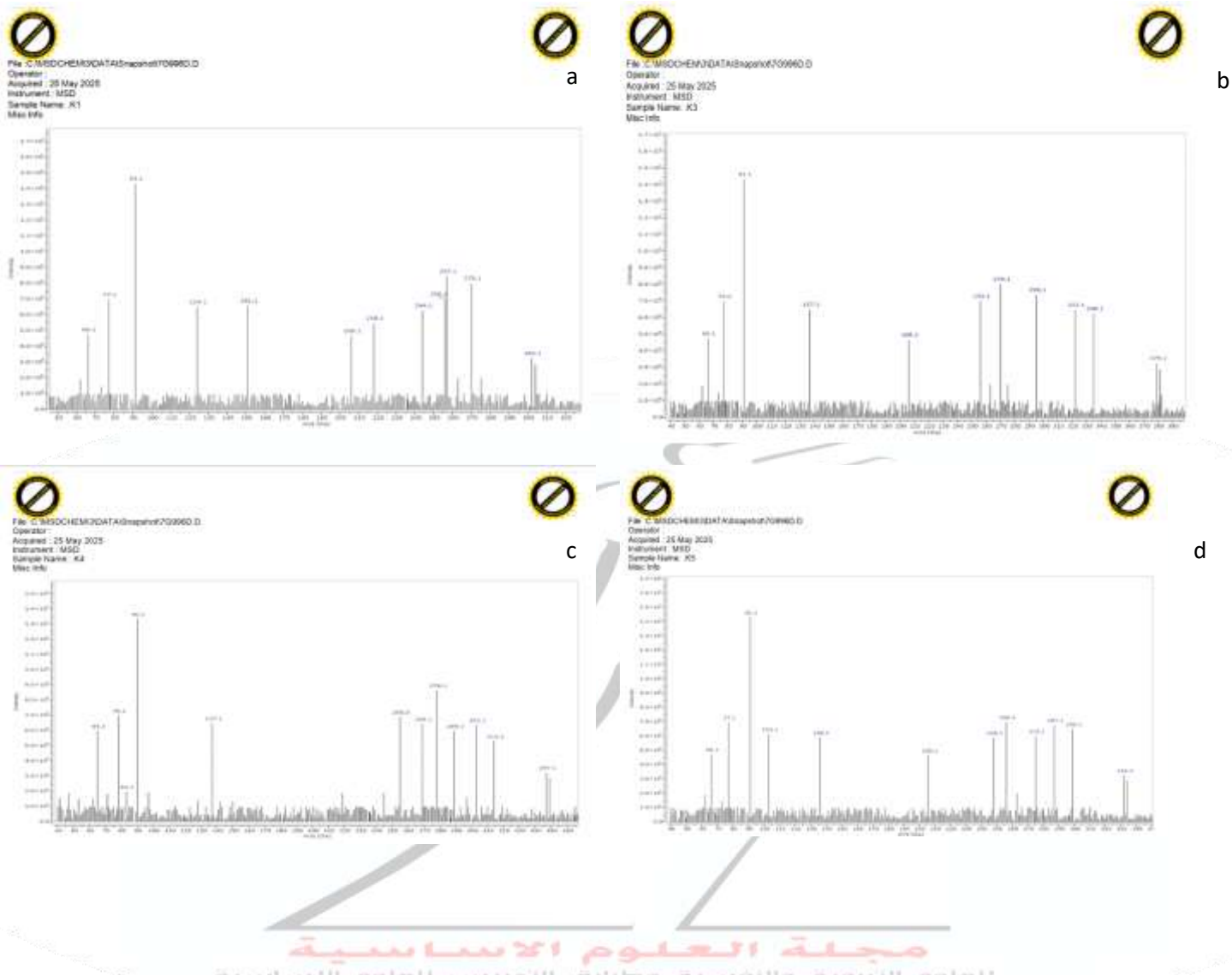

Figure 3: Mass spectrum of compounds a) cmop. K1 b) cmop. K2
c) cmop. K3 d) cmop. K4

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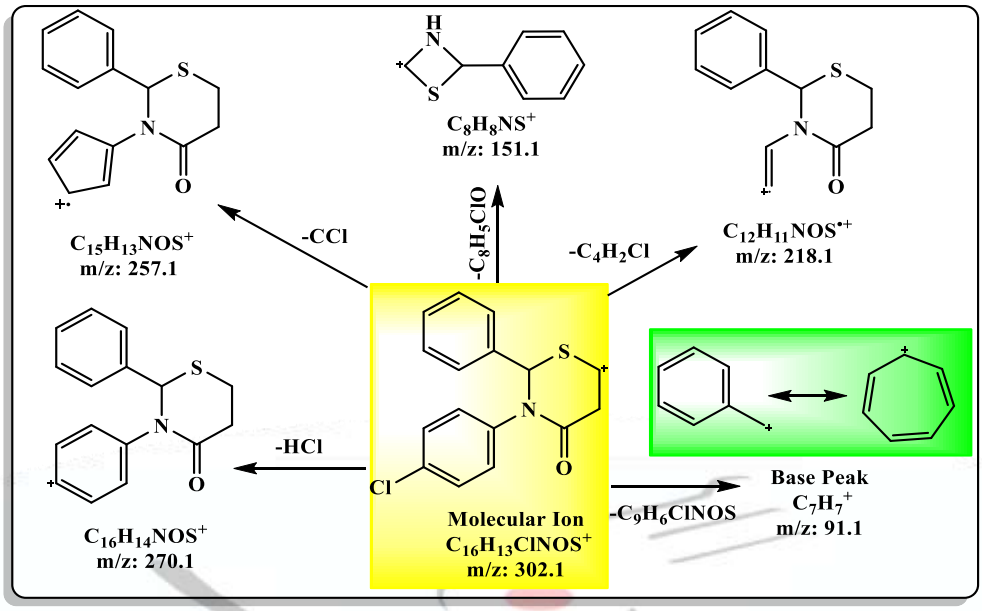

Scheme 2: Mass fragments for compound K1

5.2. Molecular Docking Results

Molecular docking was performed on all synthesized compounds (K1-K4) to predict their affinity for the target enzyme acetylcholinesterase (AChE). Analysis of the docking data indicated that all the derivatives may occupy different sites within the binding pockets of AChE, resulting in superior docking interactions compared with those of galanthamin, i.e., the reference drug, as shown in Table 4. All the compounds (K1-K4) consisted of aromatic rings, which exhibited significant hydrophobic interactions with amino acid residues located in the protein's active site. These compounds are ranked according to the amount of energy required to bind. An effective analysis was performed to determine the total interactions that each molecule makes with the binding site, calculating the total number of bonds formed between amino acid residues in the protein's active site and the synthesized derivatives (Mukhlif, 2025). Table 4 presents the obtained results based on the molecular docking analysis. In addition, Fig. 4 shows that the synthesized derivatives participate in several observed reactions that exhibit efficient proteolytic inhibition of the produced compounds. Following meticulous docking of all materials, it has been demonstrated that the K1

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compound forms two types of bonds with the amino acid residues in the protein's active site (Kadhim, 2024).

Table 4 Synthetic 1,3-thiazinan-4-one derivatives with acetylcholinesterase (AChE).

code.	Binding Affinity (kcal/mol)	Interactions	Distance (Å)	Bonding	Type of bond	Receptor	Ligand
K_1	-9.3	A:TYR121:OH - A:$K_1$1:S	٣.٧٧	H- Bond	Conventional Hydrogen Bond	A:TYR121:OH	A:$K_1$1:S
		A:SER122:OG - A:$K_1$1:O	٢.٧٩			A:SER122:OG	A:$K_1$1:O
		A:TRP84 - A:$K_1$1	٥.٤٦	Hydrophobic	π -Alkyl	A:TRP84	A:$K_1$1
		A:PHE330 - A:$K_1$1	٥.٠٩			A:PHE330	A:$K_1$1
K_2	-8.6	A:HIS440:CD2 - A:$K_2$1:O	٣.٢٠	H- Bond	Carbon Hydrogen Bond	A:HIS440:CD2	A:$K_2$1:O
		A:TYR121:OH - A:K21	٣.٦٢		π -Donor H- Bond	A:TYR121:OH	A:K21
		A:$K_2$1:S - A:TRP84	٣.٩٠	Other	π -Sulfur	A:$K_2$1:S	A:TRP84
		A:$K_2$1:S - A:TRP84	٣.٧١			A:$K_2$1:S	A:TRP84
		A:TYR121 - A:$K_2$1:Cl	٤.٨٣	Hydrophobic	π -Alkyl	A:TYR121	A:$K_2$1:Cl
		A:PHE290 - A:$K_2$1:Cl	٤.٦٦			A:PHE290	A:$K_2$1:Cl
		A:PHE330 - A:$K_2$1	٤.٨٩			A:PHE330	A:$K_2$1
K_3	-9.5	A:SER200:OG - A:$K_3$1:O	٣.١٠	H- Bond	Conventional Hydrogen Bond	A:SER200:OG	A:$K_3$1:O
		A:TYR334:OH - A:$K_3$1:O	٣.٠٨			A:TYR334:OH	A:$K_3$1:O
		A:TYR121:OH - A:$K_3$1	٣.٦٢		π -Donor H- Bond	A:TYR121:OH	A:$K_3$1
		A:TRP84 - A:$K_3$1	٥.٣٧	Hydrophobic	π -Alkyl	A:TRP84	A:$K_3$1
		A:PHE331 - A:$K_3$1:Cl	٤.٧٠			A:PHE331	A:$K_3$1:Cl
K_4	-8.8	A:HIS440:CD2 - A:$K_4$1:O	٣.١٩	H- Bond	Carbon Hydrogen Bond	A:HIS440:CD2	A:K41:O
		A:$K_4$1:C - A:ASN85:OD1	٣.٤٦		Carbon Hydrogen Bond	A:K41:C	A:ASN85:OD1
		A:TYR121:OH - A:$K_4$1	٣.٥٦		π -Donor H- Bond	A:TYR121:OH	A:K41
		A:$K_4$1:S - A:TRP84	٣.٨٢	Other	π -Sulfur	A:$K_4$1:S	A:TRP84
		A:$K_4$1:S - A:TRP84	٣.٧٦			A:$K_4$1:S	A:TRP84
		A:TYR121 - A:$K_4$1:Cl	٤.٩٧	Hydrophobic	π -Alkyl	A:TYR121	A:$K_4$1:Cl
		A:PHE290 - A:$K_4$1:Cl	٤.٧٤			A:PHE290	A:$K_4$1:Cl
		A:PHE330 - A:$K_4$1	٤.٨٣			A:PHE330	A:$K_4$1
gala.	-9.3	A:SER122:OG-A: gala..:O	٣.١١	H- Bond	Conventional H-Bond	A:SER122:OG	A: gala.:O3
		A:GLY118:CA -A: gala.:O	٣.٧٩			A:GLY118:CA	A: gala.:O2
		A: gala.:C11 A:PHE330:O	٣.٢٨			A: gala.:C11	A:PHE330:O
		A:TYR121:OH - A: gala.	٣.٥٥		π -Donor H- Bond	A:TYR121:OH	A: gala.
		.A:TRP84 - A: gala.	٥.١١	Hydrophobic	π -Alkyl	A:TRP84	A: gala.
		.A:PHE330 - A: gala.	٤.٨١			A:PHE330	A: gala.

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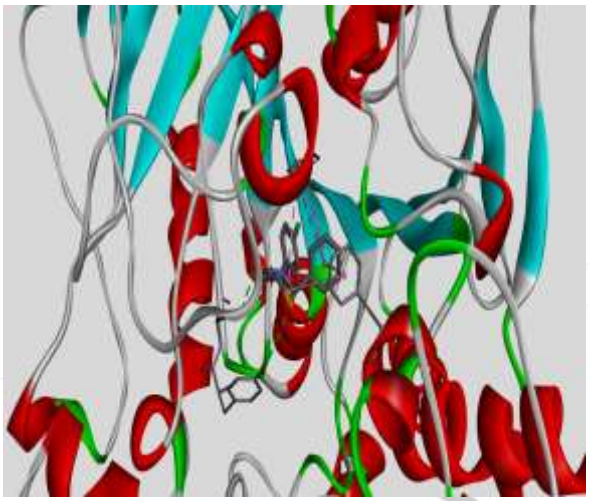
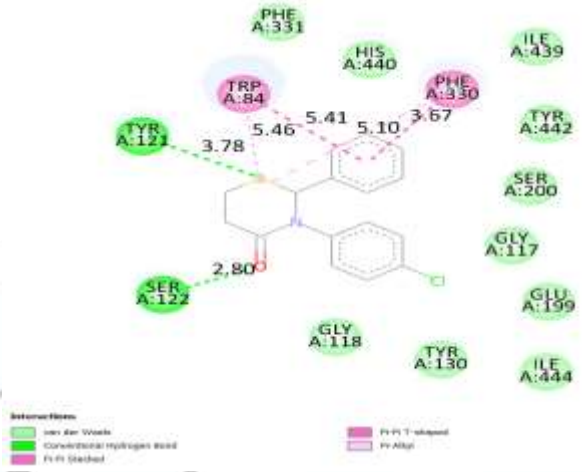
		.A:PHE330 - A: gala.	٥.٢٦			A:PHE330	A: gala.

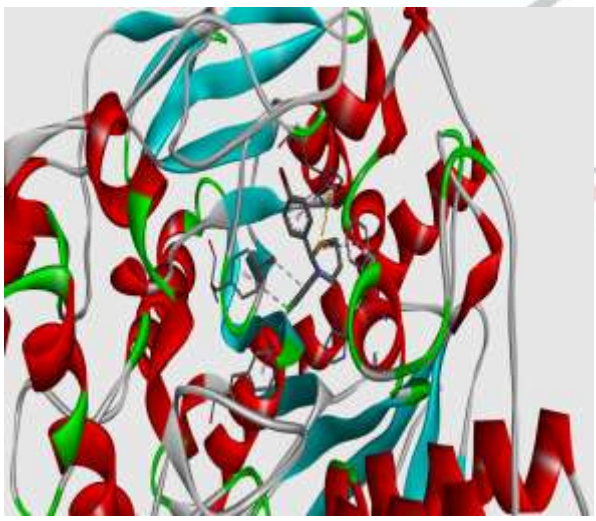


(a)



(b)

Fig4:. The interaction between K1 and (AChE). a) 2D b) 3D



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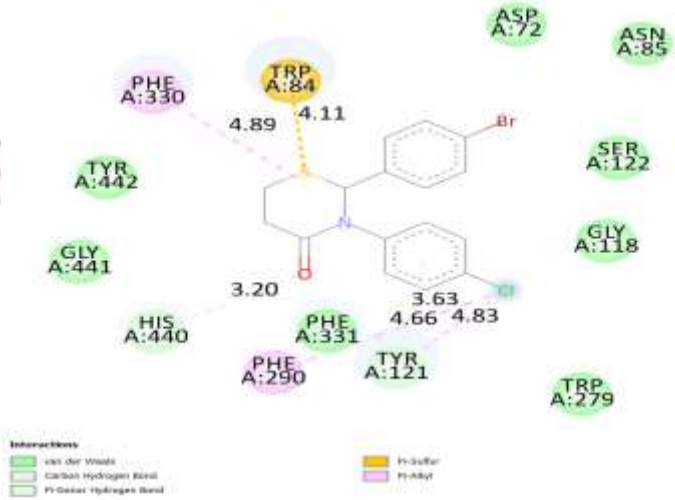

b

Fig5. The interaction between K2 and (AChE) a) 2-D, and b) 3-D

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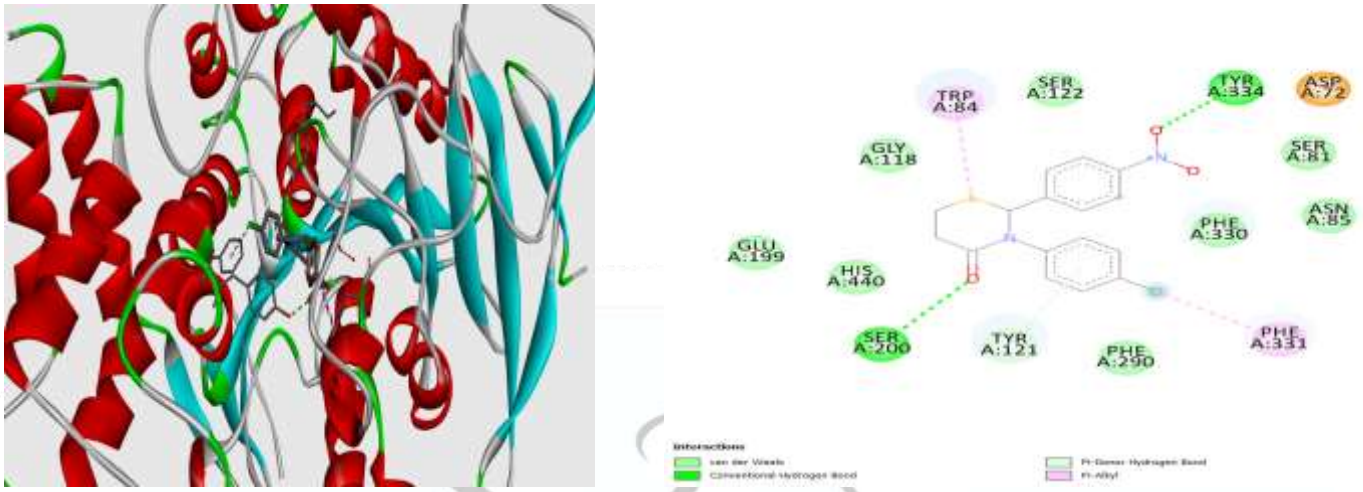

a b

Fig6. The interaction between K3 and (AChE) a) 2-D, and b) 3-D

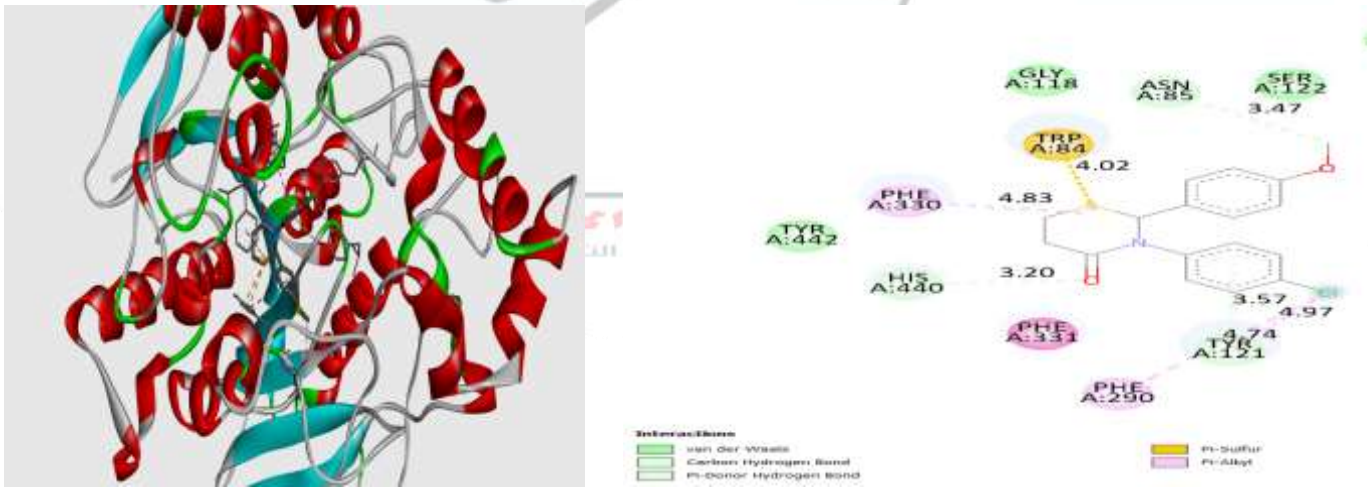

Fig 7. The interaction between K4 and (AChE) a) 2-D, and b) 3-D

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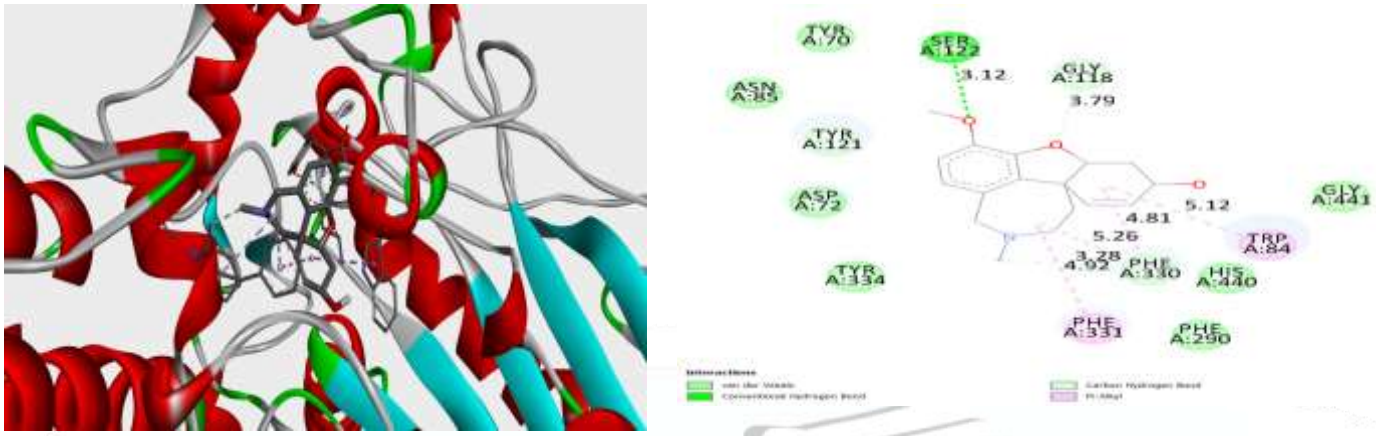

Fig 8: Interactions between the drug galanthamine and the enzyme AChE in 2D and 3D dimensions

6. Conclusion

Schiff bases (M1-M4) were synthesized using condensation from a combination of 4-chloroaniline and a substituted aromatic aldehyde. Thiazinane derivatives were synthesized via the cycloaddition of Schiff bases with 3-mercaptopropanoic acid. The identification was accomplished based on 1H-NMR, C.H.N. analysis, mass spectrometry, and Fourier transform infrared (FT-IR) spectroscopy. All of the expected chemical structures were verified by these investigations. An analysis of acetylcholinesterase (AChE) activity revealed that thiazinane derivatives had an inhibitory effect. The strong bond length and the lowest binding energy of the protein active sites were indicators of the good interactions of the thiazinane derivatives at appropriate locations with proteins, as demonstrated by molecular docking studies for protein 1EEA. Compared with the binding score of -9.3 kcal/mol attained by galanthamine, a reference medication, compound K1 achieved the highest score of -9.3 kcal/mol. It is also reasonable to assume that certain thiazinane derivatives could find use in the pharmaceutical sector as building blocks for new, improved pharmaceuticals via chemical synthesis and modification. Taken together, these findings lend credence to the idea that the synthesized thiazinane derivatives serve intriguing biological purposes and could be used therapeutically.

Declaration of competing interests

The writers of this paper affirm that they are free from any ties or financial conflicts of interest that may have seemed to impact their work.

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