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ARTICLE

Microwave-assisted synthesis of triazole derivatives conjugated with piperidine as new anti-enzymatic agents

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Abstract

The current study was aimed for the study of piperidine-based triazole compounds for their biological potential against various enzymes. A novel library of compounds, **9a-r**, having piperidine, 1,2,4-triazole, and propanamides was synthesized through consecutive steps including the formation of sulfonamide, hydrazide, 1,2,4-triazole, and thio-ether. Initially, 4-methoxybenzenesulfonyl chloride (**1**) and ethyl isonipecotate (**2**) were utilized to develop ethyl 1-(4-methoxyphenylsulfonyl)-4-piperidinecarboxylate (**3**). The product **3** was converted into respective hydrazide (**4**) which was further cyclized into 1,2,4-triazole (**5**) nucleus. A series of propanamides, **8a-r**, were synthesized from different amines, **6a-r**. These electrophiles, **8a-r**, were reacted with compound **5** under conventional and microwave-assisted protocols to acquire the library of hybrids, **9a-r**. The structural confirmations were availed by ^{1}H-NMR, ^{13}C-NMR, and IR techniques. The whole series was evaluated for biological potential against acetylcholinesterase (AChE) and α-glucosidase enzymes. The biological evaluation ranges low to high in potential for different compounds based on the structural variations of synthesized compounds. Almost all the compounds remained active against both the enzymes except a few ones. The bovine serum albumin (BSA) binding study demonstrated the flow of drug in the body, and the docking study explained the interactions responsible for active behavior of synthesized compounds.

1 | INTRODUCTION

Triazoles and their derived compounds have promising activities in the field of agriculture, medicine, biology, nano-chemistry, and material science.[2,10,18] Triazole-based compounds have the ability to act as active antiviral,[17] antifungal,[6] antibacterial, anti-inflammatory, anticonvulsant, and anticancer agents.[9,11,13,14] It is evident from literature review that the triazole-based derivatives are biologically active compounds and frequently synthesized by using conventional technique. But the microwave-assisted synthesis of triazole derivatives is not so common which we have utilized in the current work to synthesize triazole derivatives. Our group has a unique practice on the synthesis of triazole-based derivatives by using conventional as well as microwave-assisted synthetic techniques.[8,15]

The current designed product is the continuation of our previous work in order to optimize the reaction time, purity of product, economical and finally the yield by following the reaction condition by simple stirring and by using a microwave instrument. The aimed library of

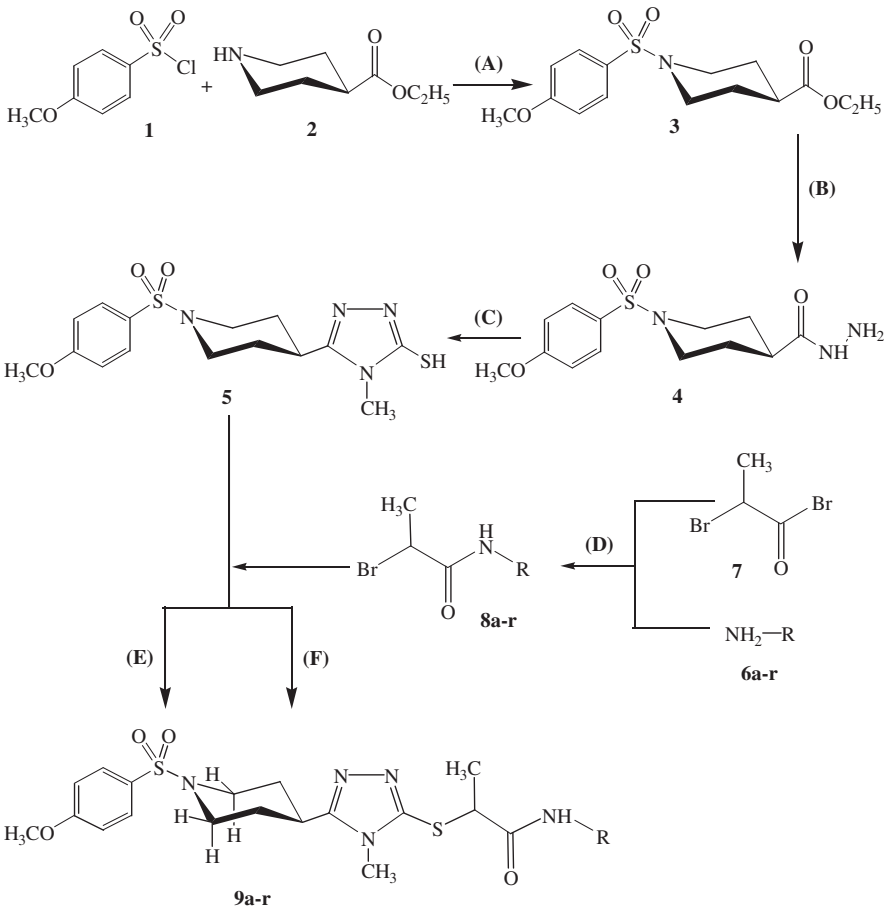
compounds was synthesized successfully by following both synthetic strategies. The better yield and minimum time revealed that the microwave-assisted technique is more powerful tool for effective synthesis of such heterocyclic compounds as compared with the conventional method.[16,19] The whole library of synthesized compounds was synthesized within 30 to 70 seconds comparative to the conventional method which has taken 10 to 15 hours (Table 2).

2 | RESULTS AND DISCUSSIONS

A series of propanamides bearing piperidine and 1,2,4-triazole ring were synthesized through conventional and microwave-assisted methods. Compounds **9a-r** were synthesized by following a series of five steps. The steps A-C involved the synthesis of 1,2,4-triazole nucleus through the subsequent synthesis of carboxylate (**3**) and hydrazide (**4**). The step D was based on the synthesis of propanamides **8a-r**, and finally, hybrids of triazole nucleus **9a-r** were synthesized by conventional as well as microwave-assisted techniques in steps E and F, respectively. The protocol of synthesis is given in Scheme 1, and the different analogues are given in Table 1. Furthermore, the synthesized compounds were subjected to the evaluation of their enzyme inhibition potential. A comparative study of conventional as well as microwave-assisted method was carried in order to judge the time span of reaction completion and yield of the synthesized compounds. It was experienced that all the compounds (**9a-r**) were synthesized in 33 to 90 seconds with 82% to 97% yield under microwave-assisted method. The results showed that the microwave-assisted methodology is better than the conventional because the conventional methodology is lazy in synthesis and also with less yield output as shown in the Table 2.

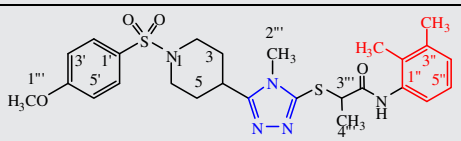
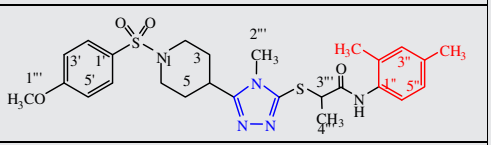
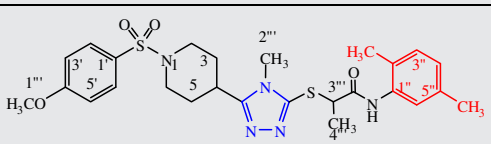
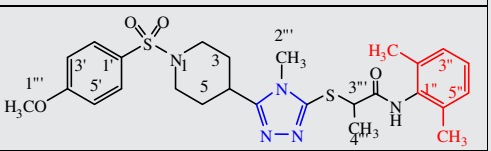
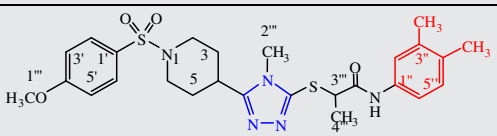
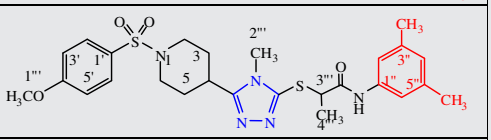
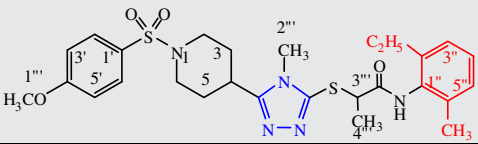
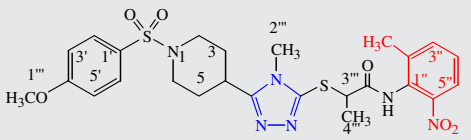
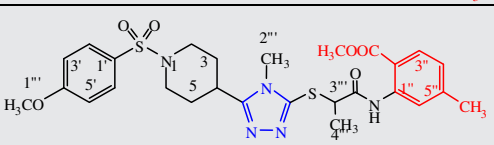
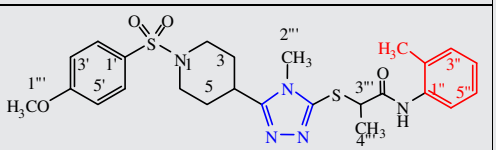
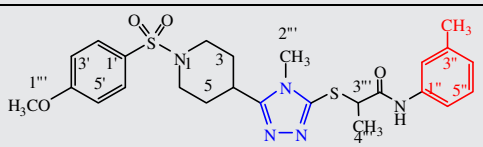
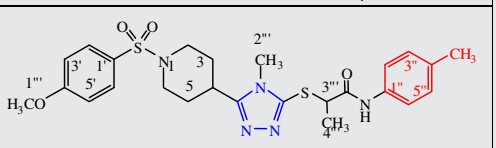
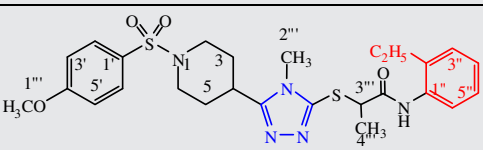
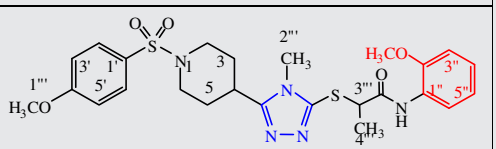
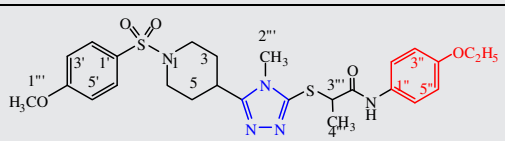
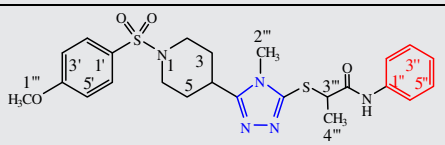
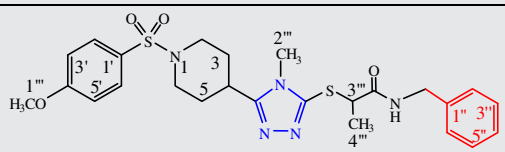
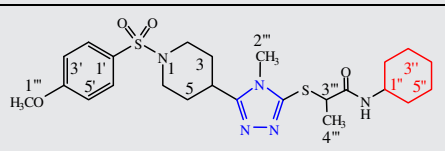
2.1 | Chemistry

For single compound discussion, one of the synthesized compounds, *N*-(3,5-dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (**9f**), is chosen. It was attained as off white amorphous solid with yield of 77% and 94% with conventional and microwave-assisted processes, respectively. The structures of all the derived compounds were confirmed by various spectroscopic techniques like ^{1}H-NMR, ^{13}C-NMR, and IR. The detailed description of **9f** is given below. The different aromatic



SCHEME 1 Synthesis of *N*-substituted-2-[(5-{1-[(4-methoxyphenyl) sulfonyl]-4-piperidinyl}-4-phenyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (**9a-r**). Reagents and conditions: (A) H_2O, 5% Na_2CO_3 soln., pH = 9-10, stirring at RT; (B) $NH_2NH_2.H_2O$, MeOH, refluxing; (C) i. MeNCS, EtOH, refluxing, ii. 10% KOH, refluxing; (D) H_2O, 5% Na_2CO_3 soln., pH = 9-10, stirring at RT; (E) DMF, LiH, stirring at RT; (F) DMF, LiH, microwaves

TABLE 1 Different synthesized analogues, **9a-r**

C.	Structure	C.	Structure
9a		**9b**	
9c		**9d**	
9e		**9f**	
9g		**9h**	
9i		**9j**	
9k		**9l**	
9m		**9n**	
9o		**9p**	
9q		**9r**	

and aliphatic protons were confirmed by ^{1}H-NMR spectra (Figures 1 and 2). At 9.81 ppm, a single peak confirmed the single proton of NH of amide group. Out of four, the two aromatic protons at position 2′ and 6′ of sulfonyl moiety resonated as doublet at 7.74 ppm with *J* value of 8.8 Hz and remaining two protons at position 3′ and 5′ also resonated as doublet at 7.02 ppm having *J* value of 8.8 Hz. The other three aromatic protons containing amide linkage resonated as two singlet at 7.72 and 6.73 of 2*H* (H-2″, H-6″) and 1*H* (H-4″), respectively. A quartet of one proton H-3‴ attached with carbon which is directly attached with carbonyl group appeared at 4.47 ppm with $J = 7.2$ Hz. Three protons of methoxy group and six protons of methyl groups attached with benzene ring were appeared as singlet at 3.90 and 2.28 ppm, respectively. The three protons of methyl group binding with nitrogen of triazole were confirmed as singlet at 3.42 ppm. The confirmation of piperidine ring was indicated through the appearance of four multiplet of nine protons at 3.86 to 3.83 (m, 2*H*, H_e-2, H_e-6), 2.62 to 2.61 (m, 1*H*, H-4), 2.54 to 2.52 (m, 2*H*, H_a-2,

TABLE 2 Comparison of conventional microwave-assisted methods

Compounds	Reaction Time		Reaction Yield %	
	Conventional, h	Microwave, s	Conventional	Microwave
9a	11	41	45	85
9b	12	44	52	87
9c	10	39	58	82
9d	14	57	73	93
9e	12	90	59	97
9f	06	63	77	94
9g	10	45	64	90
9h	11	68	75	92
9i	13	42	80	89
9j	17	53	49	86
9k	08	37	66	90
9l	12	39	64	92
9m	15	42	55	94
9n	12	49	83	91
9o	10	33	64	94
9p	08	58	65	90
9q	11	55	72	85
9r	10	56	73	92

H_a-6), and 2.08 to 1.97 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5). Three protons of methyl group attached with methine group resonated as doublet having a *J* value of 7.2 Hz at 1.64 ppm. The spectral information of ^{13}C spectroscopy was also used to confirm the structure of the compound under discussion (Figures 3–5), as ^{13}C spectrum acts as blue print of compound. The quaternary carbons present in the compound were confirmed by the peaks appearing at 169.04 (C-4′), 163.09 (C-5‴″), 157.45 (C-3‴″), 151.55 (C-6‴″), 138.66 (C-3″, C-5″), 138.09 (C-1‴″), and 127.80 (C-1′). The aromatic methine carbons in the vicinity of sulfonyl group resonated at 129.80 (C-2′, C-6′) and 114.28 (C-3′, C-5′) and that in the vicinity of amide linkage at 125.83 (C-4″) and 117.54 (C-2″, C-6″). The piperidine ring carbons were confirmed by peaks at positions 45.59 (C-2, C-6), 32.19 (C-4), and 29.13 (C-3, C-5). The carbon of methoxy group appeared at 55.63, and the carbons of four different positioning methyl groups were confirmed by peaks at 44.38 (C-3‴), 30.12 (C-2‴), 21.39 (C-5‴, C-6‴), and 16.44 (C-4‴).

2.2 | Acetyl cholinesterase inhibition potential

The AChE belongs to the family of enzymes having serine hydrolases. The current enzyme is responsible for the conversion of acetylcholine to choline which in response terminates the acetylcholine at cholinergic synapses.[3] The synthesized hybrids (**9a**-**r**) of triazole were evaluated for their potential against AChE enzyme, and their IC_{50} values are given in Table 3. The aim behind the current evaluation was the securitization of the active compound against AChE enzyme. The reference standard used in this case was Eserine. All the compounds possessed variable potential that was too high as compared with the standard. However, these compounds with the presented variety of potential against AChE have the ability to act as high ranked inhibitors of AChE.

Molecular docking study was carried out to find the binding orientation of compound **9m** with the protein in action of AChE enzyme. The ligand **9m** showed maximum inhibition potential against the AChE enzyme among all the synthesized compounds of the concerned series except compounds **9f**. SybylX-1.3 (module Surflex-Dock) was used to dock in ligand **9m** to the active site of AChE enzyme (Table 4, Figure 6). The authenticity of docked compound was checked by following the redocked into the active cite of AChE. Donepezil was extracted from the co-crystal complex 4EY7In to validate the docking methodology and then by re-docking in the same binding pocket. Experimentally, the docking poses were compared with the binding mode of donepezil in AChE.[5] This indicates that

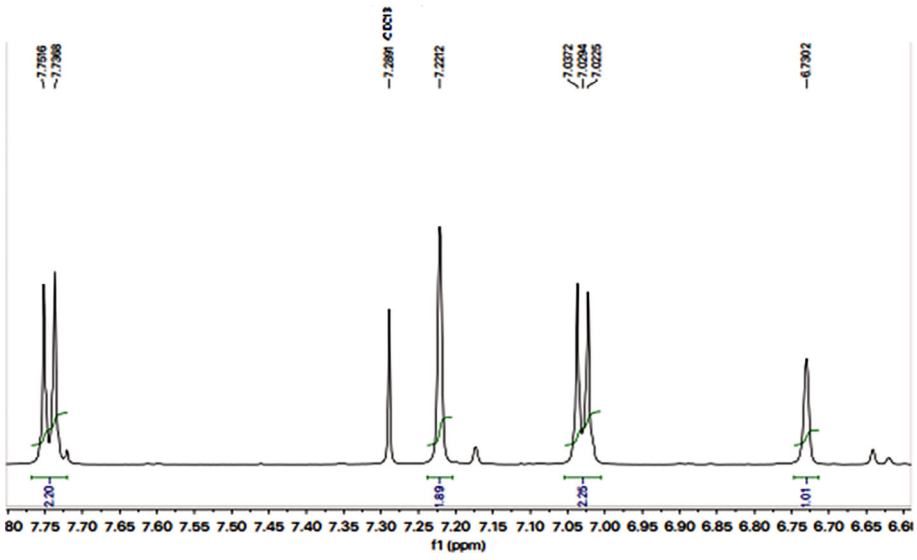


FIGURE 1 ^{1}H-NMR spectrum of compound **9f** (aromatic)

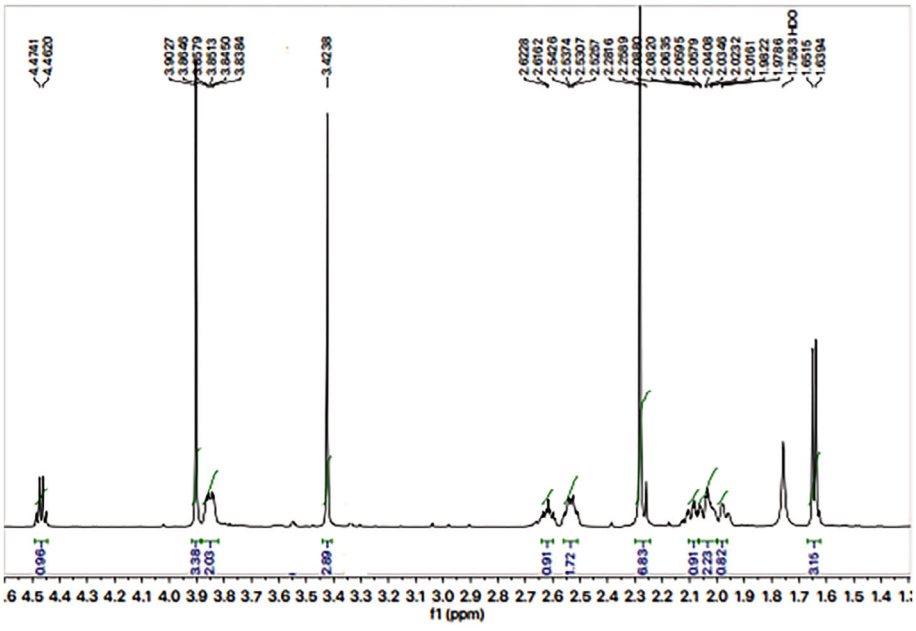


FIGURE 2 ^{1}H-NMR spectrum of compound **9f** (aliphatic)

our docking procedure is reliable. Moreover, a figure showed that the inhibitor is showing similar binding mode as found experimentally in 4EY7 complex. The graphic study of docked ligand describes that compound **9m** penetrates deeply into active cleft (CAS and PAS) of AChE enzyme. In the active site of AChE, the ligands have acquired binding position that it has developed the H-bonding with the backbone of GLY126 and ALA204. The ethyl group substituted at aromatic ring attached with amidic group deeply penetrated into the CAS region where it may have developed the hydrophobic interaction responsible for its best activity. The experimental finding like C score[a], PMF score[e], and Polar score[c] are 4.76, 39.091, and 2.50, respectively. An array of amino acids like TRP86, Ser203, Trp286, Phe295, and Phe338 showed the interaction with inhibitor drug for its better efficiency. The variability among the ligand acceptors interaction may account for potential inhibition behavior of compound **9m**.

2.3 | α-Glucosidase inhibition potential

The potential against α-glucosidase enzyme of presented compounds **9a-r** was performed to find out some active anti-α-glucosidase compounds for the cure of type 2 diabetes (Table 3). The inhibition of this enzyme by acarbose was used as reference standard. Majority of the compounds were good inhibitors which is the accumulative effect of the whole molecule. Twelve compounds

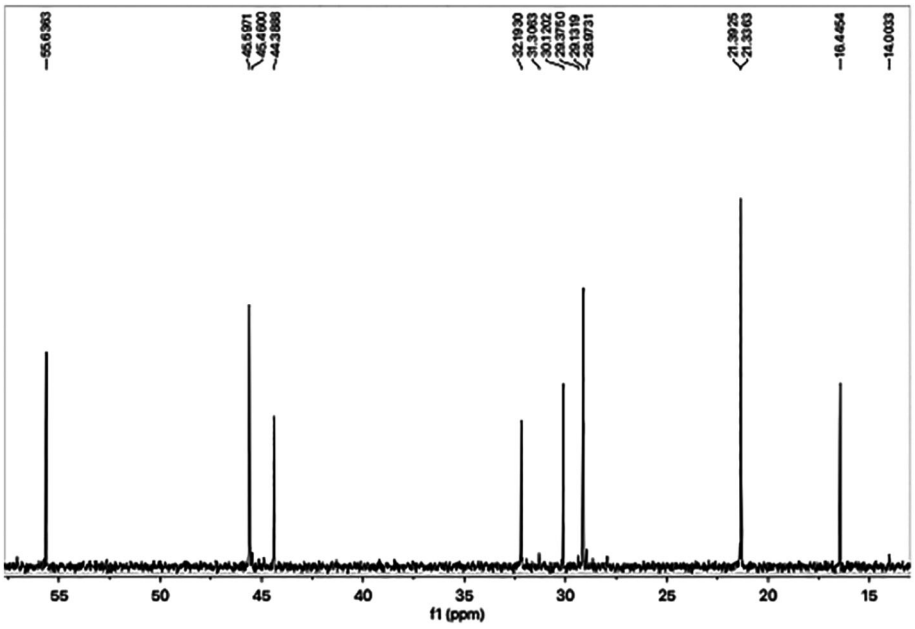


FIGURE 3 ^{13}C-NMR spectrum of compound **9f** (aliphatic)

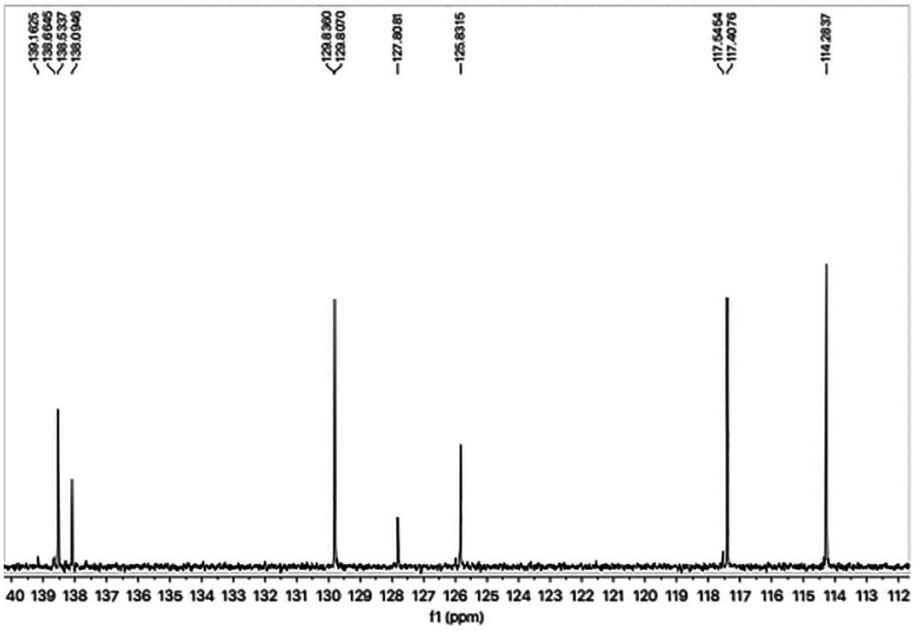


FIGURE 4 ^{13}C-NMR spectrum of compound **9f** (aromatic-up field)

expressed a very prominent activity as compared with standard. The compound **9e** revealed that it has a minimum IC_{50} value (27.52 ± 1.28) which means that it has a maximum inhibition potential as compared with the whole series of propionamides and also better than the standard. The compound **9i** was observed as least active than other active compounds because of having the highest IC_{50} (342.65 ± 1.17) but more active than acarbose. Six compounds **9b**, **9c**, **9d**, **9j**, **9n,** and **9o** were reported as inactive. For studying the SAR (structure activity relationship) between different compounds, it became evident that only a limited part of molecules is different from each other which is *N*-substituted of propanamide functionality and a remaining part was intact in all compounds. Among the six regio-isomers, **9a-f**, bearing two methyl groups on phenyl group attached with propionamide part, **9e**, having 3,4-dimethylphenyl group showed highest inhibitory potential revealed by the lowest IC_{50} value. It may be due to less steric hindrance and more binding sites with enzyme and stable complex. Among the three isomeric compounds **9j-l** containing one methyl group attached at positions 2, 3, and 4, respectively, the compound **9k** having 3-methyl phenyl group possessed good activity as compared with other two. The compounds, **9p-r**, with phenyl, benzyl, and cyclohexyl respectively without substitution also showed good inhibitory

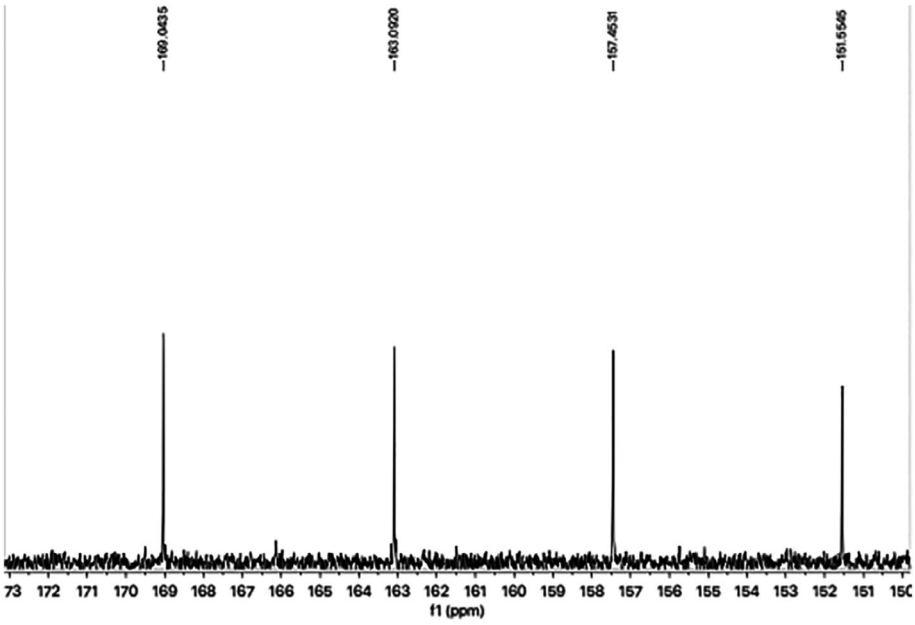


FIGURE 5 ^{13}C-NMR spectrum of compound **9f** (aromatic-down field)

TABLE 3 Biological potential of all the synthesized compounds, **9a-r**

	IC_{50} Values	
Compounds	**AChE**	**α-Glucosidase**
9a	278.46 ± 1.27	114.69 ± 1.23
9b	375.12 ± 1.15	-
9c	427.61 ± 1.19	-
9d	439.37 ± 1.24	-
9e	407.24 ± 1.22	27.52 ± 1.28
9f	261.42 ± 1.18	129.38 ± 1.34
9g	315.12 ± 1.38	45.52 ± 1.32
9h	329.85 ± 1.35	153.47 ± 1.35
9i	-	342.65 ± 1.17
9j	285.71 ± 1.23	-
9k	315.82 ± 1.27	132.63 ± 1.25
9l	349.76 ± 1.25	231.37 ± 1.23
9m	263.54 ± 1.34	146.51 ± 1.14
9n	384.62 ± 1.17	-
9o	319.43 ± 1.26	-
9p	375.16 ± 1.14	154.32 ± 1.27
9q	-	62.58 ± 1.23
9r	-	47.48 ± 1.41
Eserine	0.19 ± 0.05	
Acarbose		375.82 ± 1.76

potential. The two disubstituted phenyl part with different substituents in **9h** and **9i** were reported as active against α-glucosidase.

2.4 | BSA binding studies

The comparative BSA binding studies were carried out on the selective three compounds **9j**, **9m**, and **9r** (Table 5, Figures 7–12). The selected and designed compounds possess best binding constant values which guaranteed for their competences of showing binding with BSA. The compound **9m** showed the highest binding constant value while compound **9r** had the least one. The highest binding constant of **9m** may be because (Figure 8) of an ethyl group substituted at the ortho position of the aromatic ring responsible for the highest binding constant among synthesized series. The calculated k_q was larger than the maximum scattering collision quenching rate constant ($2 \times 10^{10}\ M^{-1}\ s^{-1}$) in dynamic quenching, which indicates that the quenching of BSA with the derivatives follows a static process, rather than a dynamic one. When small molecules bind independently to a set of equivalent sites on a macromolecule, the apparent constant (K_a) and the number of binding sites (n) can be calculated using the double reciprocal plot. The double reciprocal plots of the derivatives are shown (Figures 7 to 12). The values of K_a and n are obtained from the intercept and slope of the linear plot, respectively.

3 | EXPERIMENTAL

Unless otherwise noted, all the chemical, solvents, and reagents of analytical grade were availed by the local supplier of brand Sigma Aldrich. Analytical thin layer chromatography was used to know about the progress of

TABLE 4 Surflex score of docked ligand, compound **9m** for AChE enzyme

Docking complex = AChE-9m							
C Score[a]	Crash Score[b]	Polar Score[c]	D Score[d]	PMF Score[e]	G Score[f]	Chem Score[g]	Amino Acid Interaction
4.76	−2.15	2.50	−267.032	39.091	−254.43	−25.858	TRP86 Ser203 Trp286 Phe295 Phe338

[a]C-score is a consensus scoring which uses multiple types of scoring functions to rank the affinity of ligands.
[b]Crash-score revealing the inappropriate penetration into the binding site.
[c]Polar-score region of the ligand.
[d]D-score for chRe and van der Waals interactions between the protein and the ligand.
[e]PMF-score indicating the Helmholtz free energies of interactions for protein-ligand atom pairs (Potential of Mean Force, PMF).
[f]G-score showing hydrogen bonding, complex (ligand-protein), and internal (ligand-ligand) energies.
[g]Chem-score points for hydrogen bonding, lipophilic contact, and rotational entropy, along with an intercept term.

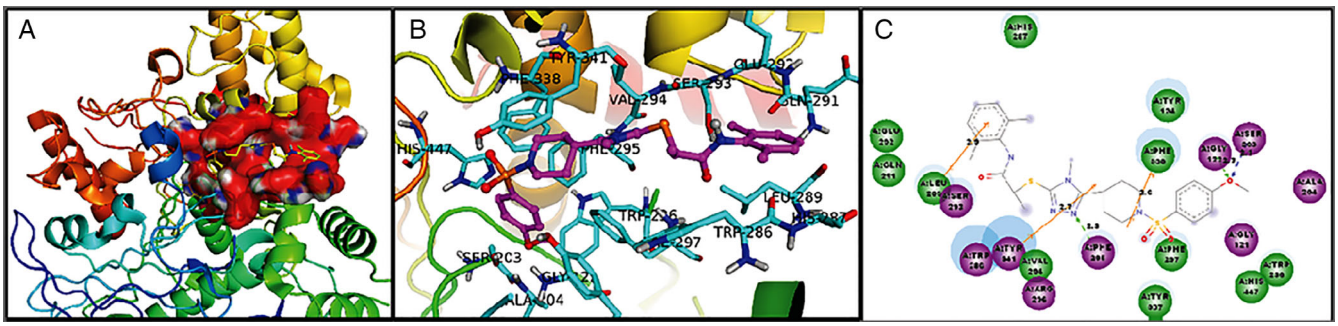


FIGURE 6 Molecular docking generated poses for selected AChE inhibitor (**9m**); (A) compound **9m** bonded within the active site of AChE enzyme; (B) binding mode of **9m** in AChE ligand binding site; (C) 2D-ligand-protein interaction diagram was generated for the best poses obtained with compound **9m** against AChE enzyme. Hydrogen bonding interactions are depicted as blue and green dotted arrows in H-bond acceptor/donner pattern, respectively. Besides, the π-π interactions are shown as orange line. The amino acids involved making key interactions with ligand are displayed as purple and green balls

Compounds	$K_{SV} \times 10^1$, M^{-1}	$k_q \times 10^{10}$, $M^{-1}\ s^{-1}$	K_a, M^{-1}	N
9j	3.9573	3.9573	5.11×10^4	1.03
9m	2.4628	2.4628	1.33×10^5	1.18
9r	1.2197	1.2197	2.43×10^3	0.84

Abbreviations: K_{SV}, Stern-Volmer quenching constant; K_q, apparent bimolecular quenching rate constant; K_a, apparent constant; N, number of binding sites.

TABLE 5 Stern-Volmer quenching constants, binding constant, and number of binding site for compounds (**9j**, **9m**, **9r**)

reaction on an aluminum plate coated with silica gel and visualized under irradiation. ^{1}H-NMR and ^{13}C-NMR were recorded by Bruker spectrometers operating at 600 and 150 MHz on Bruker AM-400 spectrometer in $CDCl_3$. The NMR data were interpreted in chemical shift (δ) in ppm while the signals multiplicities were also indicated. Coupling constant (J) was given in Hz (Hertz). The functional groups confirmation was made by using IR studies by KBr pellet method on Jasco-320-A spectrophotometer (wave number in cm^{-1}). EIMS data were availed by using JMSHX-110 spectrometer. Griffin and George apparatus were utilized to calculate the melting points. The fluorescence studies were made by using flourophotometer (Varioskan Flash 4.00.53). All the comparative data analysis under conventional and microwave-assisted techniques was presented in tabular form.

3.1 | Synthesis of ethyl 1-[(4-methoxyphenyl)sulfonyl]-4-piperidinecarboxylate (3)

Compound **3** was synthesized by room temperature stirring of the 4-methoxybenzenesulfonyl chloride (**1**;

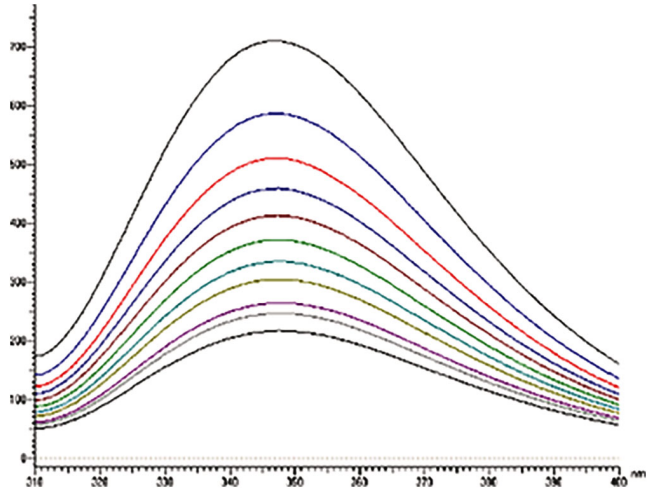


FIGURE 7 Fluorescence graph of BSA in the presence of **9j**

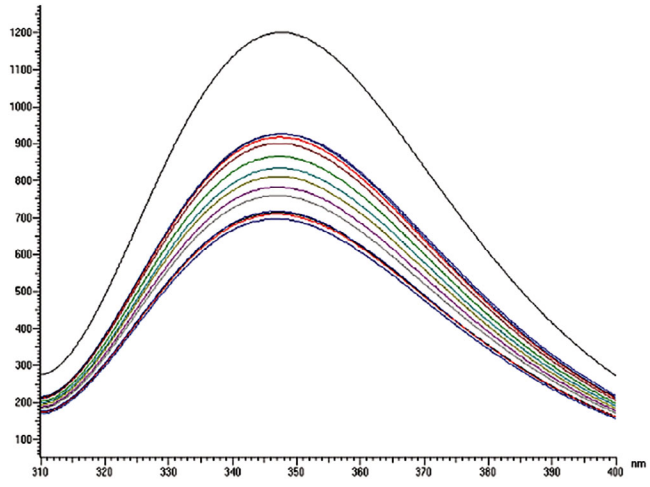


FIGURE 8 Fluorescence graph of BSA in the presence of **9m**

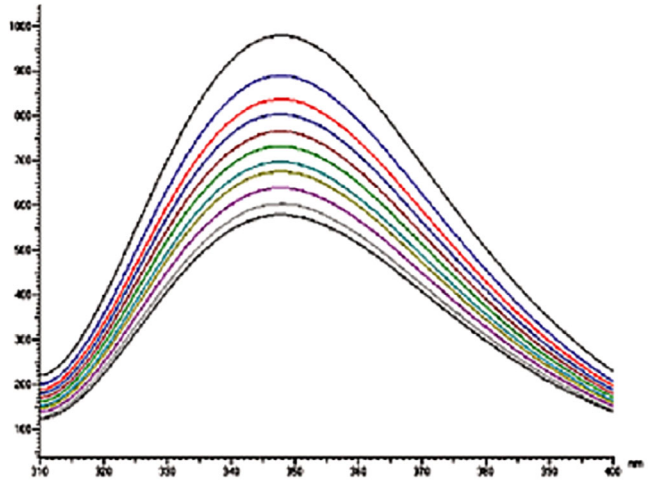


FIGURE 9 Fluorescence graph of BSA in the presence of **9r**

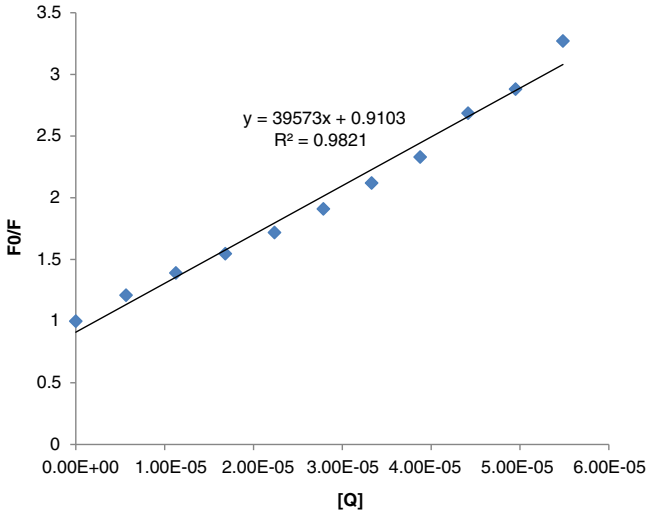


FIGURE 10 Stern-Volmer plots of **9j**

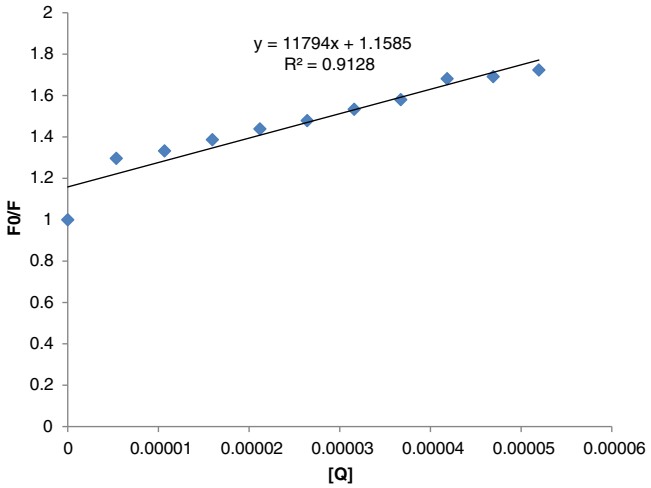


FIGURE 11 Stern-Volmer plots of **9m**

0.06 mol) with ethyl isonipecotate (**2**; 0.06 mol) in aqueous medium with 10% Na_2CO_3 solution. Analytical TLC was used to confirm the progress of reaction completion. At the end point of reaction, neutralization was achieved by dil. HCl in order to obtain the product as white precipitate. The precipitates were filtered by adding chilled water, washed, and dried at room temperature.[16]

3.2 | Synthesis of 1-(4-methoxyphenylsulfonyl)piperidine-4-carbohydrazide (4)

The synthesis of compound **4** was processed by refluxing the reactant **3** (0.05 mol) and hydrazine hydrate for

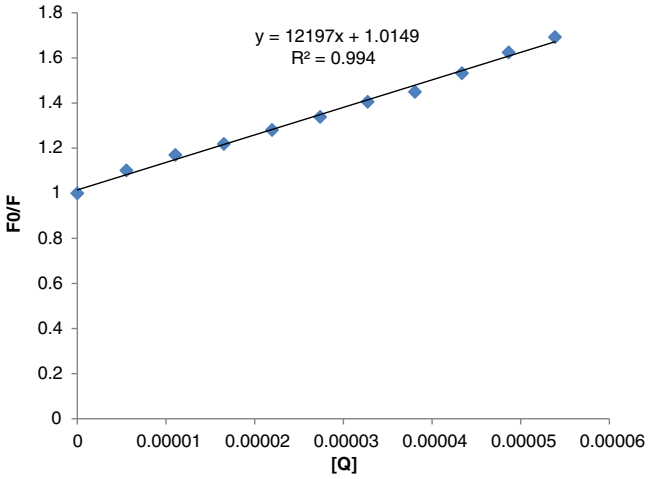


FIGURE 12 Stern-Volmer plots of **9r**

4 hours in the presence of methanol. After product confirmation by TLC, the excess solvent was evaporated, and precipitates of title compound were achieved by the addition of chilled water. The precipitates were filtered, washed, and dried.[16]

3.3 | Synthesis of 5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazole-3-thiol (5)

The title compound was synthesized by the reflux reaction of equimolar (0.0308 mol) quantities of compound **4** and methyl isothiocyanate for 1 hour. The formed intermediate was further refluxed for 1 hour with equimolar KOH. The progress of reaction was checked by TLC. On the reaction completion, the pH was adjusted at 4 to 5 by the addition of dil. HCl with continuous stirring. The title compound was precipitated, filtered, washed, and dried for further reaction.[16]

3.4 | Synthesis of *N*-(substituted)-2-bromopropanamides (8a-r)

A library of aralkyl/aryl amines (**6a-r**; 0.02 mol) and 2-bromopropionyl bromide (**7**; 0.02 mol) was reacted in distilled water on stirring for 1 to 2 hours. The pH was maintained at 9 to 10 by aqueous Na_2CO_3 solution. The amides in the various physical forms and colors were precipitated, filtered, washed, dried, and stored in low temperature environment for further reactions.[16]

3.5 | Synthesis of *N*-(substituted)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9a-r)

Method A: For the synthesis of target propanamides derivatives of 1,2,4-triazole, compound **5** with LiH was stirred at room temperature in DMF as a solvent. In the activated compound **5** (0.0005 mol), we added equimolar amounts of synthesized propanamides (**8a-r**) which worked as electrophiles with the aim to obtain the aimed products, **9a-r**. The whole mixture was stirred at room temperature for 6 to 17 hours. Thin layer chromatography was utilized to monitor the reaction conditions and progress. Finally, the products, **9a-r**, were availed through the addition of chilled distilled water. The target compounds were acquired in the form of precipitates or extracts availed by solvent extraction. The precipitates were washed, dried, and stored for further studies. The extracts were also dried and stored for further studies.

Method B: For the synthesis of target propanamides derivatives of 1,2,4-triazole, compound **5** with LiH was stirred at room temperature in DMF as a solvent. In the activated compound **5** (0.0005 mol), we added equimolar amounts of synthesized propanamides (**8a-r**) which worked as electrophiles with the aim to obtain the aimed products, **9a-r**. The whole mixture was irradiated by the microwave in microwave oven for 33 to 90 seconds. The synthesis of the compounds, **9a-r**, was performed efficiently in seconds with high purity and yield proving that the microwave synthetic strategy is more efficient and attractive. Thin layer chromatography was utilized to monitor the reaction conditions and progress. Finally, the products, **9a-r**, were availed through the addition of chilled distilled water. The target compounds were acquired in the form of precipitates or extracts availed by solvent extraction. The precipitates were washed, dried, and stored for further studies. The extracts were also dried and stored for further studies.

3.5.1 | 5-{1-[(4-Methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazole-3-thiol (5)

IR (KBr, wave number, cm^{-1}): 2800 (Ar C–H), 1611 (C═N), 1529 (Ar C═C), 1312 (S═O), 721 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 13.52 (s, 1*H*, SH), 7.70 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.17 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 3.86 (s, 3*H*, H-1‴), 3.63-3.61 (m, 2*H*, H_e-2, H_e-6), 3.37 (s, 3*H*, H-2‴), 2.83-2.80 (m, 1*H*, H-4), 2.38-2.35 (m,

2*H*, H_a-2, H_a-6), 1.97-1.95 (m, 2*H*, H_e-3, H_e-5), 1.66-1.59 (m, 2*H*, H_a-3, H_a-5); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 166.61 (C-4′), 162.63 (C-5‴), 154.31 (C-3‴), 129.63 (C-2′, C-6″), 126.63 (C-1′), 114.42 (C-3′, C-5′), 55.63 (C-1‴), 45.29 (C-2, C-6), 30.82 (C-4), 29.58 (C-2‴), 28.13 (C-3, C-5).

3.5.2 | *N*-(2,3-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9a)

White amorphous solid; yield: 88%; M.P: 190.0°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3339 (N-H), 2850 (Ar C–H), 1710 (C═O), 1650 (C═N), 1520 (Ar C═C), 1372 (CH_3), 1275 (S═O), 1150 (C–O–C), 650 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.43 (s, 1*H*, NH), 7.74 (d, J = 8.7 Hz, 2*H*, H-2′, H-6′), 7.60 (d, J = 7.9 Hz, 1*H*, H-6″), 7.06 (t, J = 7.7 Hz, 1*H*, H-5″), 7.03 (d, J = 8.7 Hz, 2*H*, H-3′, H-5′), 6.98 (d, J = 7.4 Hz, 1*H*, H-4″), 4.57 (q, J = 7.3 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.85-3.81 (m, 2*H*, H_e-2, H_e-6), 3.43 (s, 3*H*, H-2‴), 2.65-2.62 (m, 1*H*, H-4), 2.57-2.54 (m, 2*H*, H_a-2, H_a-6), 2.29 (s, 3*H*, H-5‴), 2.10 (s, 3*H*, H-6‴), 2.08-1.96 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.67 (d, J = 7.3 Hz, 3*H*, H-4‴); ^{3}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.52 (C-4′), 163.07 (C-5‴), 157.47 (C-3″), 151.53 (C-6″), 137.25 (C-1′), 135.78 (C-2″), 128.80 (C-2′, C-6′), 129.01 (C-1′), 127.81 (C-3″), 126.90 (C-6″), 125.59 (C-5″), 121.19 (C-4″), 114.27 (C-3′, C-5″), 55.63 (C-1‴), 45.53 (C-2, C-6), 43.97 (C-3‴), 32.05 (C-4), 30.05 (C-2‴), 29.11 (C-3, C-5), 20.61 (C-5‴), 16.70 (C-6‴), 13.74 (C-4‴).

3.5.3 | *N*-(2,4-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9b)

Gray white amorphous solid; yield: 90%; M.P: 153°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1520 (Ar C═C), 1370 (CH_3), 1300 (S═O), 1210 (C–O–C), 700 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.34 (s, 1*H*, NH), 7.76 (s, 1*H*, H-3″), 7.74 (d, J = 8.4 Hz, 2*H*, H-2′, H-6′), 7.03 (d, J = 8.0 Hz, 2*H*, H-3′, H-5′), 6.98-6.96 (m, 2*H*, H-5″, H-6″), 4.58 (q, J = 6.9 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.83-3.81 (m, 1*H*, H_e-2), 3.75-3.73 (m, 1*H*, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.66-2.63 (m, 1*H*, H-4), 2.60-2.57 (m, 2*H*, H_a-2, H_a-6), 2.28 (s, 3*H*, H-5‴), 2.16 (s, 3*H*, H-6‴), 2.10-2.07 (m, 1*H*, H_e-3), 2.02-1.96 (m, 3*H*, H_e-5, H_a-3, H_a-5), 1.67 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.33 (C-4′), 163.07 (C-5‴), 157.44 (C-3‴), 151.55 (C-6‴), 134.38 (C-1″), 133.56 (C-2″), 131.07 (C-6″), 129.81 (C-2′, C-6′), 129.28 (C-1′), 127.80 (C-4″), 126.89 (C-5″), 122.37 (C-3″), 114.28 (C-3′, C-5′), 55.63 (C-1‴), 45.46 (C-2, C-6), 43.82 (C-3‴), 31.85 (C-4), 30.03 (C-2‴), 29.08 (C-3, C-5), 20.80 (C-5‴), 17.99 (C-6‴), 16.61 (C-4‴).

3.5.4 | *N*-(2,5-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9c)

Off white amorphous solid; yield: 88%; M.P: 175°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3340 (N-H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1510 (Ar C═C), 1370 (CH_3), 1200 (S═O), 1250 (C–O–C), 750 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.40 (s, 1*H*, NH), 7.76 (s, 1*H*, H-6″), 7.73 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 6.86-6.84 (m, 2*H*, H-3″, H-4″), 4.60 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.82-3.80 (m, 1*H*, H_e-2), 3.74-3.72 (m, 1*H*, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.67-2.64 (m, 1*H*, H-4), 2.62-2.57 (m, 2*H*, H_a-2, H_a-6), 2.30 (s, 3*H*, H-5‴), 2.17 (s, 3*H*, H-6‴), 2.11-2.07 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.68 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.40 (C-4′), 163.07 (C-5‴), 157.46 (C-3‴), 151.58 (C-6‴), 136.09 (C-1″), 135.98 (C-2″), 130.19 (C-6″), 129.81 (C-2′, C-6′), 127.77 (C-1′), 125.98 (C-5″), 125.43 (C-3″), 122.76 (C-4″), 114.28 (C-3′, C-5′), 55.63 (C-1‴), 45.46 (C-2, C-6), 43.71 (C-3‴), 31.81 (C-4), 30.01 (C-2‴), 29.09 (C-3, C-5), 21.13 (C-4‴), 17.65 (C-5‴), 16.56 (C-4‴).

3.5.5 | *N*-(2,6-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9d)

Off white amorphous solid; yield: 90%; M.P: 231.0°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2800 (Ar C–H), 1690 (C═O), 1610 (C═N), 1520 (Ar C═C), 1300 (CH_3), 1270 (S═O), 1125 (C–O–C), 730 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.30 (s, 1*H*, NH), 7.74 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.08-7.03 (m, 3*H*, H-3″, H-4″, H-5″), 7.02 (d, J = 8.7 Hz, 2*H*, H-3′, H-5′), 4.57 (q, J = 7.3 Hz, 1*H*, H-3‴), 3.88 (s, 3*H*, H-1‴), 3.81-3.78 (m, 2*H*, H_e-2, H_e-6), 3.47 (s, 3*H*, H-2‴), 2.69-2.65 (m, 1*H*, H-4), 2.62-2.58 (m, 2*H*, H_a-2, H_a-6), 2.07 (s, 6*H*, H-5‴, H-6‴), 2.06-1.99 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.69 (d, J = 7.3 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$,

150 MHz, δ [ppm]): 169.59 (C-4′), 163.08 (C-5‴′), 157.33 (C-3‴′), 151.54 (C-6‴′), 135.32 (C-1″), 133.91 (C-2″, C-6″), 129.79 (C-2′, C-6′), 128.00 (C-3″, C-5″), 127.79 (C-1′), 127.06 (C-4″), 114.28 (C-3′, C-5′), 55.62 (C-1‴), 45.42 (C-2, C-6), 43.90 (C-3‴), 31.93 (C-4), 31.32 (C-2‴), 29.05 (C-3, C-5), 18.14 (C-5‴, C-6‴).

3.5.6 | *N*-(3,4-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9e)

Off white amorphous solid; yield: 90%; M.P: 189.2°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2820 (Ar C–H), 1650 (C═O), 1600 (C═N), 1520 (Ar C═C), 1310 (S═O), 1200 (C–O–C), 630 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.92 (s, 1*H*, NH), 7.75 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.36-7.36 (m, 1*H*, H-6″), 7.30-7.29 (m, 1*H*, H-5″), 7.05 (s, 1*H*, H-2″), 7.03 (d, J = 8.7 Hz, 2*H*, H-3′, H-5′), 4.46 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.86-3.82 (m, 2*H*, H_e-2, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.63-2.61 (m, 1*H*, H-4), 2.63-2.55 (m, 2*H*, H_a-2, H_a-6), 2.23 (s, 3*H*, H-5‴), 2.21 (s, 3*H*, H-6‴), 2.10-1.98 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.66 (d, J = 7.0 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 168.85 (C-4′), 163.08 (C-5‴′), 157.41 (C-3‴′), 151.59 (C-6‴′), 137.05 (C-1″), 135.99 (C-3″), 132.37 (C-4″), 129.81 (C-2′, C-6′), 127.80 (C-1′), 120.89 (C-6″), 117.12 (C-2″), 115.87 (C-5″), 114.27 (C-3′, C-5′), 55.63 (C-1‴), 45.56 (C-2, C-6), 44.26 (C-3‴), 32.14 (C-4), 30.10 (C-2‴), 29.09 (C-3, C-5), 19.81 (C-5‴), 19.15 (C-6‴), 16.41 (C-4‴).

3.5.7 | *N*-(3,5-Dimethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9f)

Off white amorphous solid; yield: 87%; M.P: 190.3°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2830 (Ar C–H), 1710 (C═O), 1620 (C═N), 1530 (Ar C═C), 1310 (CH_3), 1230 (S═O), 1140 (C–O–C), 715 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.81 (s, 1*H*, NH), 7.74 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.72 (s, 2*H*, H-2″, H-6″), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 6.73 (s, 1*H*, H-4″), 4.47 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.86-3.83 (m, 2*H*, H_e-2, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.62-2.61 (m, 1*H*, H-4), 2.54-2.52 (m, 2*H*, H_a-2, H_a-6), 2.28 (s, 6*H*, H-5‴, H-6‴), 2.08-1.97 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.64 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.04 (C-4′), 163.09 (C-5‴′), 157.45 (C-3‴′), 151.55 (C-6‴′), 138.66 (C-3″, C-5″), 138.09 (C-1″), 129.80 (C-2′, C-6′), 127.80 (C-1′), 125.83 (C-4″), 117.54 (C-2″, C-6″), 114.28 (C-3′, C-5′), 55.63 (C-1‴), 45.59 (C-2, C-6), 44.38 (C-3‴), 32.19 (C-4), 30.12 (C-2‴), 29.13 (C-3, C-5), 21.39 (C-5‴, C-6‴), 16.44 (C-4‴).

3.5.8 | *N*-(2-Ethyl-6-methylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9g)

White amorphous solid; yield: 89%; M.P: 202.3°C; HRMS: $[M]^{\bullet+}$ 557.2120 (Calcd. for $C_{27}H_{35}N_5O_4S_2$; 557.2130); IR (KBr, wave number, cm^{-1}): 3339 (N–H), 2825 (Ar C–H), 1700 (C═O), 1610 (C═N), 1525 (Ar C═C), 1350 (CH_3), 1250 (S═O), 1150 (C–O–C), 720 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.26 (s, 1*H*, NH), 7.74 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.13 (t, J = 7.5 Hz, 1*H*, H-4″), 7.06-7.03 (m, 2*H*, H-3″, H-5″), 7.01 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 4.60 (q, J = 7.3 Hz, 1*H*, H-3‴), 3.88 (s, 3*H*, H-1‴), 3.81-3.77 (m, 2*H*, H_e-2, H_e-6), 3.48 (s, 3*H*, H-2‴), 2.68-2.63 (m, 1*H*, H-4), 2.61-2.59 (m, 2*H*, H_a-2, H_a-6), 2.46 (q, J = 7.5 Hz, 2*H*, H-6‴), 2.11 (s, 3*H*, H-5‴), 2.08-2.01 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.68 (d, J = 7.3 Hz, 3*H*, H-4‴), 1.04 (t, J = 7.2 Hz, 3*H*, H-7‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.83 (C-4′), 163.08 (C-5‴′), 157.34 (C-3‴′), 151.55 (C-6‴′), 141.13 (C-1″), 135.79 (C-2″), 133.27 (C-6″), 129.81 (C-2′, C-6′), 128.20 (C-1′), 128.06 (C-3″), 127.41 (C-4″), 126.37 (C-5″), 114.30 (C-3′, C-5′), 55.61 (C-1‴), 45.41 (C-2, C-6), 43.74 (C-3‴), 31.93 (C-4), 30.12 (C-2‴), 29.06 (C-3, C-5), 24.78 (C-6‴), 18.15 (C-5‴), 17.00 (C-4‴), 14.55 (C-7‴).

3.5.9 | *N*-(2-Methyl-6-nitrophenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9h)

Light yellow amorphous solid; yield: 89%; M.P: 175°C; HRMS: $[M]^{\bullet+}$ 574.1659 (Calcd. for $C_{25}H_{30}N_6O_6S_2$; 574.1668); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2820 (Ar C–H), 1670 (C═O), 1600 (C═N), 1500 (Ar C═C), 1350 (CH_3), 1310 (S═O), 1200 (C–O–C), 690 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 10.07 (s, 1*H*, NH), 7.74 (d, J = 8.5 Hz, 2*H*, H-2′, H-6′), 7.46 (m, 2*H*, H-3″, H-5″), 7.26 (t, J = 7.7 Hz, 1*H*, H-4″), 7.01 (d, J = 8.1 Hz, 2*H*, H-3′, H-5′), 4.60 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.89 (s, 3*H*, H-1‴), 3.82-3.79 (m, 2*H*, H_e-2, H_e-6), 3.49 (s, 3*H*, H-2‴), 2.70-2.68 (m, 1*H*, H-4), 2.62-2.58 (m, 2*H*, H_a-2, H_a-6), 2.29 (s, 6*H*, H-5‴, H-6‴), 2.11-2.05 (m, 4*H*,

H_e-3, H_e-5, H_a-3, H_a-5), 1.66 (d, J = 7.1 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.67 (C-4′), 163.05 (C-5⁗), 157.57 (C-3⁗), 151.40 (C-6⁗), 146.15 (C-1″), 137.62 (C-2″), 135.06 (C-6″), 129.82 (C-2′, C-6′), 128.77 (C-1′), 127.77 (C-3″), 126.53 (C-5″), 122.52 (C-4″), 114.26 (C-3′, C-5′), 63.72 (C-5‴), 55.62 (C-1‴), 45.48 (C-2, C-6), 43.48 (C-3‴), 31.95 (C-4), 30.19 (C-2‴), 29.01 (C-3, C-5), 18.49 (C-5‴, C-6‴), 16.52 (C-4‴).

3.5.10 | Methyl 2-({2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanoyl}amino)-5-methylbenzoate (9i)

White amorphous solid; yield: 85%; M.P: 167.0°C; HRMS: $[M]^{\bullet+}$ 587.1864 (Calcd. for $C_{27}H_{33}N_5O_6S_2$; 587.1872); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2820 (Ar C–H), 1690 (C═O), 1600 (C═N), 1500 (Ar C═C), 1310 (CH_3), 1250 (S═O), 1150 (C–O–C), 690 (C-H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 7.73 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.42 (d, J = 7.2 Hz, 1*H*, H-6″), 7.37-7.34 (m, 1*H*, H-5″), 7.23 (s, 1*H*, H-3″), 7.02 (d, J = 8.9 Hz, 2*H*, H-3′, H-5′), 4.35 (q, J = 7.3 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.85-3.83 (m, 2*H*, H_e-2, H_e-6), 3.51 (s, 3*H*, H-5‴), 3.40 (s, 3*H*, H-2‴), 3.26 (s, 3*H*, H-6‴), 2.66-2.58 (m, 3*H*, H-4, H_a-2, H_a-6), 2.07-1.89 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.60 (d, J = 7.1 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 168.52 (C-4′), 163.17 (C-7⁗), 163.01 (C-5⁗), 155.28 (C-3⁗), 152.61 (C-2″), 138.53 (C-1″), 137.89 (C-4″), 129.81 (C-1′), 129.75 (C-2′, C-6′), 128.66 (C-6″), 128.05 (C-3″), 127.46 (C-5″), 114.26 (C-3′, C-5′), 55.62 (C-1‴), 48.23 (C-5‴), 45.39 (C-2, C-6), 45.53 (C-3‴), 31.76 (C-4), 28.99 (C-3, C-5), 28.48 (C-2‴), 16.88 (C-4‴), 14.98 (C-6‴).

3.5.11 | 2-[(5-{1-[(4-Methoxyphenyl) sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]-*N*-(2-methylphenyl)propanamide (9j)

White amorphous solid; yield: 88%; M.P: 196.5°C; HRMS: $[M]^{\bullet+}$ 529.1809 (Calcd. for $C_{25}H_{31}N_5O_4S_2$; 529.1817); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2810 (Ar C–H), 1680 (C═O), 1600 (C═N), 1530 (Ar C═C), 1300 (CH_3), 1250 (S═O), 1150 (C–O–C), 710 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.48 (s, 1*H*, NH), 7.95 (d, J = 8.0 Hz, 1*H*, H-6″), 7.73 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.18-7.14 (m, 2*H*, H-4″, H-5″), 7.05-7.02 (m, 3*H*, H-3′, H-5′, H-3″), 4.60 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.83-3.81 (m, 1*H*, H_e-2), 3.74-3.72 (m, 1*H*, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.67-2.64 (m, 1*H*, H-4), 2.63-2.57 (m, 2*H*, H_a-2, H_a-6), 2.22 (s, 3*H*, H-5‴), 2.11-2.06 (m, 2*H*, H_e-3, H_e-5), 2.03-1.96 (m, 2*H*, H_a-3, H_a-5), 1.67 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 166.99 (C-4′), 163.08 (C-5⁗), 159.01 (C-3⁗), 157.73 (C-6⁗), 136.15 (C-1″), 130.42 (C-2″), 129.80 (C-2′, C-6′), 129.29 (C-1′), 128.00 (C-6″), 126.42 (C-3″), 124.88 (C-5″), 122.39 (C-4″), 114.28 (C-3′, C-5′), 55.63 (C-1‴), 45.34 (C-2, C-6), 43.78 (C-3‴), 31.83 (C-4), 30.02 (C-2‴), 28.99 (C-3, C-5), 18.11 (C-5‴), 16.56 (C-4″‘).

3.5.12 | 2-[(5-{1-[(4-Methoxyphenyl) sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]-*N*-(3-methylphenyl)propanamide (9k)

Off white amorphous solid; yield: 86%; M.P: 170°C; HRMS: $[M]^{\bullet+}$ 529.1809 (Calcd. for $C_{25}H_{31}N_5O_4S_2$; 529.1817); IR (KBr, wave number, cm^{-1}): 3338 (N–H), 2800 (Ar C–H), 1680 (C═O), 1600 (C═N), 1510 (Ar C═C), 1370 (CH_3), 1350 (S═O), 1200 (C–O–C), 770 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.92 (s, 1*H*, NH), 7.75 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.74 (s, 1*H*, H-2″), 7.36 (d, J = 8.1 Hz, 1*H*, H-6″), 7.17 (t, J = 7.7 Hz, 1*H*, H-5″), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 6.90 (d, J = 7.5 Hz, 2*H*, H-4″), 4.47 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.86-3.82 (m, 2*H*, H_e-2, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.63-2.62 (m, 1*H*, H-4), 2.56-2.54 (m, 2*H*, H_a-2, H_a-6), 2.33 (s, 3*H*, H-5‴), 2.10-1.98 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.66 (d, J = 7.3 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.05 (C-4′), 163.09 (C-5⁗), 157.45 (C-3⁗), 151.60 (C-6⁗), 138.76 (C-1″), 138.20 (C-3″), 129.82 (C-2′, C-6′), 128.66 (C-6″), 127.78 (C-1′), 124.87 (C-2″), 120.23 (C-5″), 116.76 (C-4″), 114.28 (C-3′, C-5′), 55.64 (C-1‴), 45.57 (C-2, C-6), 44.29 (C-3‴), 32.15 (C-4), 30.11 (C-2‴), 29.10 (C-3, C-5), 21.46 (C-5‴), 16.41 (C-4‴).

3.5.13 | 2-[(5-{1-[(4-Methoxyphenyl) sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]-*N*-(4-methylphenyl)propanamide (9l)

White amorphous solid; yield: 85%; M.P: 177°C; HRMS: $[M]^{\bullet+}$ 529.1809 (Calcd. for $C_{25}H_{31}N_5O_4S_2$; 529.1817); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2820 (Ar C–H), 1690 (C═O), 1610 (C═N), 1500 (Ar C═C), 1350 (CH_3), 1300 (S═O), 1250 (C–O–C), 630 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.91 (s, 1*H*, NH), 7.75 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.46 (d, J = 8.4 Hz, 2*H*, H-2″, H-6″), 7.10 (d, J = 8.2 Hz, 2*H*, H-3″, H-5″), 7.03 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 4.66 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.85-3.81 (m, 2*H*, H_e-2, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.64-2.60 (m, 1*H*, H-4), 2.58-2.55 (m, 2*H*, H_a-2, H_a-6), 2.31

(s, 3*H*, H-5‴), 2.10-1.98 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.65 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 168.87 (C-4′), 163.08 (C-5‴), 157.43 (C-3‴), 151.59 (C-6‴), 135.77 (C-1″), 133.61 (C-4″), 129.82 (C-2′, C-6′), 129.31 (C-2″, C-6″), 127.78 (C-1′), 119.60 (C-3″,C-5″), 114.27 (C-3′, C-5′), 55.64 (C-1‴), 45.55 (C-2, C-6), 44.26 (C-3‴), 32.10 (C-4), 30.11 (C-2‴), 29.08 (C-3, C-5), 20.84 (C-5‴), 16.42 (C-4‴).

3.5.14 | *N*-(2-Ethylphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9m)

Off white amorphous solid; yield: 90%; M.P: 185.7°C; HRMS: $[M]^{\bullet+}$ 543.1959 (Calcd. for $C_{26}H_{33}N_5O_4S_2$; 543.1974); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2800 (Ar C–H), 1670 (C═O), 1600 (C═N), 1570 (Ar C═C), 1360 (CH_3), 1200 (S═O), 1150 (C–O–C), 745 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.44 (s, 1*H*, NH), 7.73 (d, J = 8.7 Hz, 2*H*, H-2′, H-6′), 7.17 (d, J = 7.4 Hz, 1*H*, H-6″), 7.10-7.07 (m, 3*H*, H-3″, H-4″, H-5″), 7.01 (d, J = 8.7 Hz, 2*H*, H-3′, H-5′), 4.58 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.89 (s, 3*H*, H-1‴), 3.82-3.80 (m, 1*H*, H_e-2), 3.75-3.73 (m, 1*H*, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.66-2.65 (m, 1*H*, H-4), 2.64-2.51 (m, 2*H*, H_a-2, H_a-6), 2.09 (q, J = 6.5 Hz, 2*H*, H-5‴), 2.02-1.89 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.66 (d, J = 7.2 Hz, 3*H*, H-4‴), 1.08 (t, J = 7.5 Hz, 3*H*, H-6‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.62 (C-4′), 163.07 (C-5‴), 157.48 (C-3‴), 151.56 (C-6‴), 135.54 (C-1″), 135.35 (C-2″), 129.77 (C-2′, C-6′), 128.62 (C-6″), 127.81 (C-1′), 126.26 (C-5″), 125.20 (C-4″), 123.31 (C-6″), 114.27 (C-3′, C-5′), 55.62 (C-1‴), 45.44 (C-2, C-6), 43.80 (C-3‴), 31.82 (C-4), 30.03 (C-2‴), 29.12 (C-3, C-5), 24.39 (C-5‴), 16.69 (C-4‴), 14.16 (C-6‴).

3.5.15 | *N*-(2-Methoxyphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9n)

Off white amorphous solid; yield: 88%; M.P: 168.5°C; HRMS: $[M]^{\bullet+}$ 545.1758 (Calcd. for $C_{26}H_{33}N_5O_5S_2$; 545.1767); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1500 (Ar C═C), 1350 (CH_3), 1250 (S═O), 1150 (C–O–C), 700 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.40 (s, 1*H*, NH), 7.73 (d, J = 8.9 Hz, 2*H*, H-2′, H-6′), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 6.93-6.91 (m, 2*H*, H-5″, H-6″), 7.84-6.83 (m, 2*H*, H-3″, H-4″), 4.60 (q, J = 7.1 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.83 (s, 3*H*, H-5‴), 3.81-3.75 (m, 2*H*, H_e-2, H_e-6), 3.41 (s, 3*H*, H-2‴), 2.63-2.61 (m, 1*H*, H-4), 2.59-2.54 (m, 2*H*, H_a-2, H_a-6), 2.12-2.07 (m, 2*H*, H_e-3, H_e-5), 2.02-1.88 (m, 2*H*, H_a-3, H_a-5), 1.66 (d, J = 7.2 Hz, 3*H*, H-4‴‘); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.08 (C-4′), 163.06 (C-5‴), 157.37 (C-3‴), 150.50 (C-6‴), 141.13 (C-2‴), 145.00 (C-1″), 129.82 (C-2′, C-6′), 127.90 (C-1′), 123.92 (C-3″), 120.74 (C-6″), 119.75 (C-4″), 114.27 (C-3′, C-5′), 110.12 (C-5″), 55.62 (C-1‴), 45.45 (C-2, C-6), 44.65 (C-3‴), 31.89 (C-4), 29.98 (C-2‴), 29.00 (C-3, C-5), 16.71 (C-4‴).

3.5.16 | *N*-(4-Ethoxyphenyl)-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9o)

Chocolate brown amorphous solid; yield: 90%; M.P: 178.5°C; HRMS: $[M]^{\bullet+}$ 559.1917 (Calcd. for $C_{26}H_{33}N_5O_5S_2$; 559.1923); IR (KBr, wave number, cm^{-1}): 3341 (N–H), 2800 (Ar C–H), 1630 (C═O), 1600 (C═N), 1510 (Ar C═C), 1300 (S═O), 1230 (C–O–C), 760 (C-H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 9.88 (s, 1*H*, NH), 7.72 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.47 (d, J = 9.0 Hz, 2*H*, H-2″, H-6″), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 6.82 (d, J = 9.0 Hz, 2*H*, H-3″, H-5″), 4.44 (q, J = 7.2 Hz, 1*H*, H-3‴), 4.00 (q, J = 6.9 Hz, 2*H*, H-5‴), 3.89 (s, 3*H*, H-1‴), 3.84-3.80 (m, 2*H*, H_e-2, H_e-6), 3.42 (s, 3*H*, H-2‴), 2.63-2.56 (m, 1*H*, H-4), 2.54-2.51 (m, 2*H*, H_a-2, H_a-6), 2.09-1.94 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.64 (d, J = 7.2 Hz, 3H, H-4‴), 1.40 (t, J = 6.9 Hz, 3H, H-6‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 168.75 (C-4′), 163.07 (C-5‴), 157.45 (C-3‴), 155.51 (C-4″), 151.47 (C-6‴), 131.47 (C-1″), 129.79 (C-2′, C-6′), 127.72 (C-1′), 121.12 (C-3″,C-5″), 114.71 (C-2″, C-6″), 114.28 (C-3′, C-5′), 63.72 (C-5″‘), 55.63 (C-1″‘), 45.56 (C-2, C-6), 44.44 (C-3″‘), 32.10 (C-4), 31.30 (C-2″‘), 29.08 (C-3, C-5), 16.55 (C-4″‘), 14.75 (C-6″‘).

3.5.17 | 2-[(5-{1-[(4-Methoxyphenyl) sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]-*N*-phenylpropanamide (9p)

White amorphous solid; yield: 89%; M.P: 180.0°C; HRMS: $[M]^{\bullet+}$ 515.1653 (Calcd. for $C_{24}H_{29}N_5O_4S_2$; 515.1661); IR (KBr, wave number, cm^{-1}): 3337 (N–H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1550 (Ar C═C), 1300 (CH_3), 1250 (S═O), 1150 (C–O–C), 700 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 10.08 (s, 1*H*, NH), 7.73 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.58 (d, J = 7.6 Hz, 2*H*, H-2″, H-6″), 7.29 (t, J = 7.6 Hz, 2*H*, H-3″, H-5″), 7.08 (t, J = 7.3 Hz, 1*H*, H-4″), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 4.47 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.85-3.80 (m, 2*H*, H_e-2, H_e-6), 3.43

(s, 3*H*, H-2‴), 2.63-2.60 (m, 1*H*, H-4), 2.57-2.51 (m, 2*H*, H_a-2, H_a-6), 2.10-2.00 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.66 (d, J = 7.2 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.09 (C-4′), 163.09 (C-5‴), 157.49 (C-3‴), 151.54 (C-6‴), 138.34 (C-1″), 129.78 (C-2′, C-6′), 128.84 (C-2″, C-6″), 127.79 (C-1′), 124.04 (C-4″), 119.83 (C-3″, C-5″), 114.28 (C-3′, C-5′), 55.64 (C-1‴), 45.54 (C-2, C-6), 44.36 (C-3‴), 32.15 (C-4), 30.13 (C-2‴), 27.95 (C-3, C-5), 16.43 (C-4‴).

3.5.18 | *N*-Benzyl-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9q)

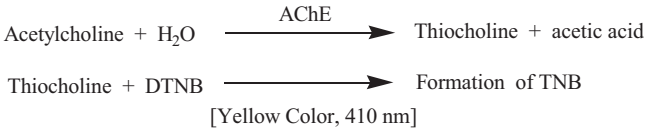
Lemon yellow sticky solid; yield: 87%; M.P: 170.5°C; HRMS: $[M]^{\bullet+}$ 529.1809 (Calcd. for $C_{25}H_{31}N_5O_4S_2$; 529.1817); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1450 (Ar C═C), 1350 (CH_3), 1200 (S═O), 1150 (C–O–C), 730 (C-H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 12.65 (s, 1*H*, NH), 8.57 (d, J = 8.2 Hz, 2*H*, H-2″, H-6″), 8.10-8.07 (m, 1*H*, H-4″), 7.66 (d, J = 8.7 Hz, 2*H*, H-2′, H-6′), 7.05-7.02 (m, 2*H*, H-3″, H-5″), 7.00 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 4.18 (q, J = 6.6 Hz, 1*H*, H-3‴), 3.88 (s, 3*H*, H-1‴), 3.80-3.78 (m, 1*H*, H_e-2), 3.74-3.71 (m, 1*H*, H_e-6), 3.34 (s, 3*H*, H-2‴), 2.97 (s, 2*H*, H-5‴), 2.57-2.54 (m, 1*H*, H-4), 2.50-2.46 (m, 2*H*, H_a-2, H_a-6), 2.27-2.16 (m, 2*H*, H_e-3, H_e-5), 2.03-1.92 (m, 2*H*, H_a-3, H_a-5), 1.65 (d, J = 6.9 Hz, 3*H*, H-4‴); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 169.07 (C-4′), 163.08 (C-5‴), 158.09 (C-3‴), 154.02 (C-6‴), 148.86 (C-1″), 140.21 (C-2″, C-6″), 129.74 (C-2′, C-6′), 127.58 (C-1′), 122.74 (C-3″, C-5″), 118.98 (C-4″), 114.26 (C-3′, C-5′), 55.63 (C-1‴), 45.79 (C-2, C-6), 45.43 (C-3‴), 35.07 (C-5‴), 32.47 (C-2‴), 31.45 (C-4), 28.54 (C-3, C-5), 16.83 (C-4‴).

3.5.19 | *N*-Cyclohexyl-2-[(5-{1-[(4-methoxyphenyl)sulfonyl]-4-piperidinyl}-4-methyl-4*H*-1,2,4-triazol-3-yl)sulfanyl]propanamide (9r)

Brown amorphous solid; yield: 88%; M.P: 173.0°C; HRMS: $[M]^{\bullet+}$ 521.2122 (Calcd. for $C_{24}H_{35}N_5O_4S_2$; 521.2130); IR (KBr, wave number, cm^{-1}): 3340 (N–H), 2800 (Ar C–H), 1650 (C═O), 1600 (C═N), 1520 (Ar C═C), 1350 (CH_3), 1250 (S═O), 1100 (C–O–C), 700 (C–H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ [ppm]): 7.73 (d, J = 8.8 Hz, 2*H*, H-2′, H-6′), 7.02 (d, J = 8.8 Hz, 2*H*, H-3′, H-5′), 4.22 (q, J = 7.2 Hz, 1*H*, H-3‴), 3.90 (s, 3*H*, H-1‴), 3.84-3.82 (m, 2*H*, H_e-2, H_e-6), 3.69-3.67 (m, 1*H*, H-1″), 3.44 (s, 3*H*, H-2‴), 2.68-2.65 (m, 1*H*, H-4), 2.63-2.56 (m, 2*H*, H_a-2, H_a-6), 2.11-2.00 (m, 4*H*, H_e-3, H_e-5, H_a-3, H_a-5), 1.57 (d, J = 7.2 Hz, 3*H*, H-4‴), 1.35-1.27 (m, 4*H*, H-2″, H-6″), 1.22-1.15 (m, 4*H*, H-3″, H-5″), 1.07-1.05 (m, 2*H*, H-4″); ^{13}C-NMR ($CDCl_3$, 150 MHz, δ [ppm]): 170.01 (C-4′), 163.17 (C-5‴), 157.20 (C-3″), 152.66 (C-6‴), 129.82 (C-2′, C-6″), 127.88 (C-1′), 114.27 (C-3′, C-5′), 55.63 (C-1‴), 48.38 (C-1″), 45.52 (C-2, C-6), 44.47 (C-3‴), 32.60 (C-2″, C-6″), 32.14 (C-3″, C-5″), 31.23 (C-4), 30.11 (C-2‴), 29.09 (C-3, C-5), 25.46 (C-4″), 16.91 (C-4‴).

3.5.20 | Acetyl cholinesterase inhibition assay

The potential of synthesized array of 1,2,4-triazole hybrids was checked against the acetyl cholinesterase by following the reported Ellman's procedure with necessary modifications.[4] The basic for the reported method is development of yellow TNB by DTNB along with thiocholine. The reference inhibitor that was utilized to access the potential of synthesized compounds, **9a-r**, was Eserine. The assay could be well justified by the given below equation.



Each well in the 96-well plate was filled with 60 μL buffer solution of pH 7.7 followed by the addition of synthesized compounds 10 μL. The whole mixture was scanned at 405 nm by maintaining the temperature at 37°C. By the addition of acetylthiocholine (10 μL) followed by the addition of 10 μL DTNB (0.5 mM), the reaction was started. At 37°C for 16 to 30 minutes, the mixture was incubated, and absorbance was noted at 405 nm by using 96-well plate reader Synergy HT, Biotek, USA. The whole experiment was performed in triplicate and % inhibition was measured by following the given formula.

$$\textbf{Inhibition}\ (\%) = \frac{\textbf{Control} - \textbf{Test}}{\textbf{Control}} \times \mathbf{100}$$

Control is the absorbance without test sample while test is in the presence of sample. By using Ez-Fit software (Perrella Scientific Inc. Amherst, Massachusetts), the IC_{50} values were calculated.

3.5.21 | α-Glucosidase inhibition assay

The α-glucosidase inhibition potential was calculated by following the reported procedure with necessary modifications.[12] A mixture of 70 μL phosphate buffer saline of pH 6.8, 10 μL of enzyme and test sample each was taken in 96-well plate. The whole mixture was incubated at

37°C for 10 minutes, and absorbance was calculated at 400 nm. After incubation, 10 μL *p*-nitrophenyl glucopyranoside (0.5 mM) was added as a substrate. The absorbance after incubation period was again calculated at 400 nm with the aid of Synergy HT microplate reader. The whole experiment was carried out in triplicate. The % inhibition and IC_{50} values were calculated in the similar way as described for cholinesterase enzymes.

3.5.22 | Statistical analysis

All the calculations were made in triplicate, the data were obtained in triplicate, and statistical analysis was performed by Microsoft Excel 2010. Results were presented as mean ± SEM.

3.5.23 | Computational studies

The interaction of synthesized compounds with AChE active site was determined by using the RCSB data bank for protein in order to collect co-crystal 3D structure.[5] *SYBYL-X 1.3* was used for structure preparation of all the available proteins, while for the types of atoms, charges, and missing hydrogen atoms, an AMBER 7 FF99 force field was utilized. Sybyl-X 1.3 was availed to SKETCH module and built 3D-structures of active inhibitors with consideration of using Tripo force field with Gasteigere Hückel atomic charge. The reported protocol of surflex-Docked module of SybylX-1.3 was utilized to do the molecular docking studies of synthesized compounds with few modifications.[7]

3.5.24 | BSA binding interactions using fluorescence measurements

The BSA binding studies were carried out to find out the inter action of synthesized series of compounds with protein. The flurometric titrations were used to calculate the quenching constant. A mixture of test compound along with buffer and BSA solution was mixed. The mixture was excited at 295 nm. The intensity of synthesized compounds alone and with test compound was measured at 336 nm. The site selective binding was measured with and in absence of site markers (ibuprofen or warfarin).[1]

4 | CONCLUSION

The current study was performed to synthesize the compounds bearing heterocyclic moieties together in one unit and then to evaluate their enzyme inhibition potential. The synthesized compounds were structurally elaborated through ^{1}H-NMR, ^{13}C-NMR, and IR techniques. This potential was further elaborated through molecular docking study. The BSA binding study revealed the excellent binding potential of the synthesized compounds.

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