



ORIGINAL ARTICLE

Synthesis, molecular docking and ADMET studies of bis-benzimidazole-based thiadiazole derivatives as potent inhibitors, *in vitro* α -amylase and α -glucosidase



Shoaib Khan ^a, Shahid Iqbal ^{b,*}, Wajid Rehman ^{c,*}, Nadia Hussain ^{d,e},
Rafaqat Hussain ^c, Mazloom Shah ^f, Farhan Ali ^c, Ahmed M. Fouda ^g, Yousaf Khan ^h,
Ayed A. Dera ⁱ, Mohammed Issa Alahmdi ^j, Ali Bahadur ^k, Hanan A. Al-ghulikah ^l,
Eslam B. Elkaeed ^{m,*}

^a Department of Chemistry, Abbottabad University of Science and Technology (AUST) Abbottabad, Pakistan

^b Department of Chemistry, School of Natural Sciences (SNS), National University of Science and Technology (NUST), H-12, Islamabad 46000, Pakistan

^c Department of Chemistry, Hazara University, Mansehra 21120, Pakistan

^d Department of Pharmaceutical Sciences, College of Pharmacy, Al Ain University, Al Ain, UAE

^e AAU Health and Biomedical Research Center, Al Ain University, Abu Dhabi, UAE

^f Department of Chemistry, Faculty of Science, Grand Asian University Sialkot, Pakistan

^g Chemistry Department, Faculty of Science, King Khalid University, Abha 61413, Saudi Arabia

^h Department of Chemistry, COMSATS University Islamabad Campus-45550, Islamabad, Pakistan

ⁱ Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Saudi Arabia

^j Department of Chemistry, Faculty of Science, University of Tabuk, Tabuk 71491, Saudi Arabia

^k Department of Chemistry, College of Science and Technology, Wenzhou-Kean University, Wenzhou 325060, China

^l Department of Chemistry, College of Science, Princess Nourah bint Abdulrahman University, P.O. Box 84428, Riyadh 11671, Saudi Arabia

^m Department of Pharmaceutical Sciences, College of Pharmacy, AlMaarefa University, Riyadh 13713, Saudi Arabia

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* Corresponding authors.

E-mail addresses: shahidiqbal@hzu.edu.cn (S. Iqbal), sono_waj@gmail.com (W. Rehman), ikaeed@mcst.edu.sa (E.B. Elkaeed).

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KEYWORDS

Bis-benzimidazole;
Thiadiazole;
 α -amylase;
 α -glucosidase;
SAR ADMET;
Molecular docking

Abstract Different research synthetic methods have been developed recently for the synthesis of bis-benzimidazole analogs to investigate various biological significances. In this present study, an attempt was made to synthesize a new series of bis-benzimidazole analogs in a fast and efficient method. A variety of spectroscopic techniques, including ^{13}C NMR, ^1H NMR, and HREI-MS, were used to establish the existence of every synthesized scaffold. Molecular docking profiles were also carried out to ascertain the binding interactions of the compounds. All derivatives (**1–18**) were evaluated for their biological potential to investigate the inhibitory activity of α -amylase and α -glucosidase through SAR study. Almost all derivatives were found to be engaged in a highly promising activity when compared to referenced drug acarbose ($\text{IC}_{50} = 8.24 \pm 0.08 \mu\text{M}$), in this regard among the tested series analog **9** ($\text{IC}_{50} = 0.10 \pm 0.50$ and $0.20 \pm 0.50 \mu\text{M}$ respectively), showed excellent activity. Moreover, ADME predictions were also studied for potent compounds, exhibited drug like properties.

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1. Introduction

A chronic condition called diabetes mellitus prevents the body from properly metabolizing proteins, carbs, and lipids. It also causes several issues in the body that lead to hyperglycemia (American Diabetes Association, 2013). Diabetes presently affects 4.4% of the global population, up from 2.8% in 2000. Diabetes is going to impact approximately 366 million people globally by 2030 (Wild et al., 2004; Sacks, 1997). A range of synthetic oral hypoglycemic medicines, such as sulfonylureas, biguanides, and alpha-glucosidase inhibitors, are used to decrease elevated blood glucose levels. Unfortunately, their longer usage has shown more of its different negative effects (Edwin et al., 2006) such as hypoglycemia, headache, nausea, and dizziness (Chaudhury et al., 2017). The negative effects made it necessary to discover innovative, efficient, and safer substitutes that have the highest priority (Es-Safi et al., 2020). Researchers are actively focusing on heterocyclic compounds because to its potential for being efficient, accessible, and having fewer adverse effects. The current study also based on heterocyclic compounds such benzimidazole-based thiadiazole derivatives. The primary aim of this study was to investigate the inhibitory potential of synthesized scaffolds in contrast to both α -amylase and α -glucosidase enzymes. In compared to other heterocyclic compounds, the benzimidazole ring got considerably more attention. Its ring is commonly referred to as “privileged” due to its wide range of biological significance. The structure of benzimidazole and the chemistry of their ligands are of great interest to researchers (Mechchate et al., 2020; Bonnett, 1963). Similar products, including thiabendazole, misonidazole, omeprazole, astemizole, clotrimazole, and cimetidine were a significant source of biologically active drugs as well as they have some other positive effects in agricultural and veterinary fields (Al-Muhaimeed, 1997). Due to the presence of various groups on the benzimidazole ring, drugs containing benzimidazole moiety exhibit a wide range of pharmacological profiles such as Bactericidal (Carcanague et al., 2002), analgesic (Aghatabay et al., 2007; Demirayak et al., 2005; Gaba et al., 2014; Sondhi et al., 2006; Achar et al., 2010), fungicidal (Lezcano et al., 2002; Sun et al., 2021; Sun et al., 2021), antiviral (Tewari and Mishra, 2006; Basha, 2022; Ibba et al., 2022; Huo et al., 2021), and HIV-1 infectivity inhibition (Gardiner et al., 1995). Benzimidazole and thiadiazole moieties have been extensively studied and found with better inhibitory potential against varied infections, especially diabetes mellitus. Therefore in the project, the aim was to synthesize and evaluate bis-benzimidazole-based thiadiazole analogs and screen against α -amylase and α -glucosidase. They were also found effective inhibitors against both enzymes. Moreover, binding interactions were confirmed through molecular docking studies. Besides, rationales of the current

analog-A (Aroua et al., 2021) and analog-B (Zawawi et al., 2016) have been mentioned in the comparison activity of synthesized analogs with previously reported compounds as shown in Fig. 1.

2. Results and discussion

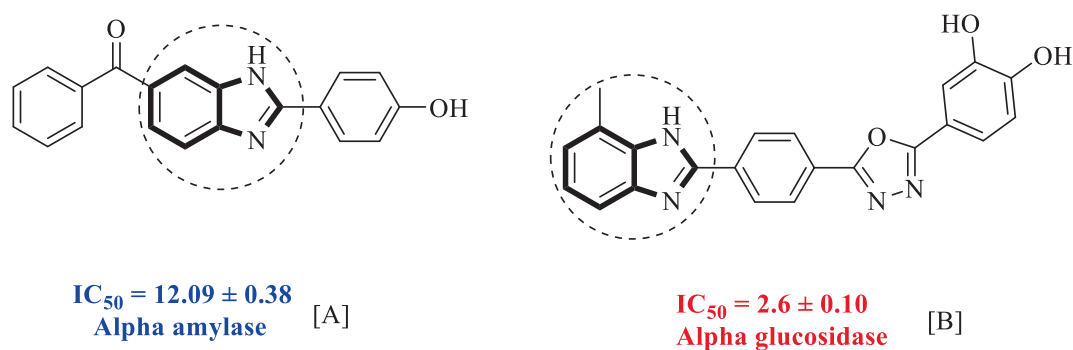
2.1. Chemistry

The synthesis of bis-benzimidazole-containing thiadiazole derivatives was conducted using a stepwise reactions technique (**1–18**). Initially, benzimidazole bearing aldehyde group (**I**) and thiosemicarbazide were mixed in methanol and refluxed in the reaction mixture for about 3 h in the presence of sodium acetate to obtain Schiff base an intermediate (yields = 88% **II**). Upon addition of iodine in 1,4-dioxane in the presence of potassium carbonate, the reaction was refluxed for about 12 h, afforded benzimidazole-based thiadiazole containing an amine group (yields = 72% **III**). Compound (**III**) was further refluxed for about 6 h with s-substituted benzimidazole-based ketone derivatives in ethanol followed by the addition of acetic acid gives bis-benzimidazole bearing thiadiazole derivatives as shown in the Scheme 1.

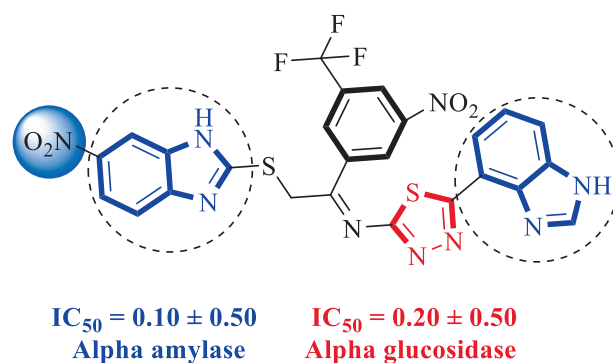
2.2. Spectral analysis

A structure interpretation of the represented compound-10 was identified and their proton, as well as carbon peaks, were identified through NMR spectroscopic technique. The proton value of the represented compound has appeared at different ppm which indicates the shielded and de-shielded region of the proton, carbon as well as HREI-MS.

^1H NMR (600 MHz, $\text{DMSO-}d_6$): δ . The first proton appeared at 11.87 showing a singlet for NH of benzimidazole ring bearing nitro group similarly, another proton appeared at 11.62 also showing a singlet for NH of second benzimidazole ring. –OH proton appeared at 9.57 showing singlet while other aromatic proton appeared at 8.78 showing doublet with coupling constant (J) 7.1, and another proton appeared at 8.51 showing doublet with $J = 6.8$ Hz. Similarly, 8.36 shows singlet for Benzimidazole-H and 7.57 showing doublet, with $J = 6.7$ Hz, of Benzimidazole-H, 7.33 showing singlet for

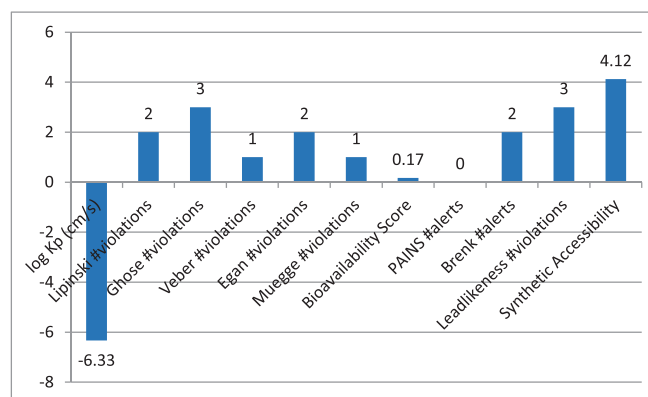


Previously reported analog as alpha amylase and alpha glucosidase inhibitor



Newly synthetic analog as alpha amylase and alpha glucosidase inhibitor

Fig. 1 Rationale of the current study.



Scheme 1 Thiadiazole derivatives based on the synthesis of bis-benzimidazoles (1–18).

2H of Benzimidazole-H and 7.10 doublet with $J = 8.1$ Hz, of Benzimidazole-H, 6.86 displayed as a doublet with $J = 8.1$ Hz, for 2H of Benzimidazole-H, 6.59 doublet with $J = 7.1$ Hz of Benzimidazole-H and 3.83 singlets for 2H of -SCH₂ and ¹³C NMR (150 MHz, DMSO *d*₆): showing in descending order δ 162.2, 159.9, 149.6, 148.9, 148.0, 147.1, 145.0, 144.3, 142.0,

140.9, 139.8, 139.4, 134.1, 128.7, 128.4, 127.6, 125.9, 123.4, 121.5, 118.6, 115.5, 109.4, 100.9, 55.6 as well as HR EI-MS: m/z calcd for C₂₄H₁₄Cl₂N₈O₃S₂ [M]⁺ 596.0630; Found: 596.0518. The detailed spectral analysis of all the compounds (1–18) has been incorporated in the [supplementary information](#).

3. Structure-activity relationship (SAR)

3.1. α -amylase and α -glucosidase inhibitory profile

Biological profiles of synthesized analogs were compared with one another and the standard drug acarbose. Most of the analogs were found with good to moderate activity when compared to the standard drug. Variation in biological activity might be the position, numbers and type of substituents attached among trifluoro, nitro and hydroxyl-containing analogs were found with excellent potential. Comparisons of analogs based on their substituents and position are given below.

Nitro and trifluoro-substituted analogs were arranged for comparison study due to their excellent biological profile when compared to their potential with standard drug acarbose ($IC_{50} = 3.66 \pm 0.12$ and $4.85 \pm 0.11 \mu\text{M}$). These analogs showed a varied range of inhibitory profiles such as **1** ($IC_{50} = 1.10 \pm 0.10$ and $1.80 \pm 0.10 \mu\text{M}$), **4** ($IC_{50} = 1.20 \pm 0.20$ and $2.0 \pm 0.20 \mu\text{M}$), **9** ($IC_{50} = 0.10 \pm 0.50$ and $0.20 \pm 0.50 \mu\text{M}$) and **11** (3.40 ± 0.10 and 4.70 ± 0.10). Among the screens analog **9** was found with remarkable potential while others showed good to moderate activity might be the presence of the trifluoro group which makes strong hydrogen bonding and nitro moiety also dominate the negative charge at *meta*-position therefore the over effect was found greater as compared to other analogs.

Chloro-substituted analogues **3** ($IC_{50} = 3.40 \pm 0.10$ and $5.80 \pm 0.10 \mu\text{M}$), **12** ($IC_{50} = 6.10 \pm 0.10$ and $7.70 \pm 0.10 \mu\text{M}$), and **17** ($IC_{50} = 2.80 \pm 0.10$ and $3.70 \pm 0.10 \mu\text{M}$), were shown to have action similar to that of the medication acarbose ($IC_{50} = \mu\text{M}$). The position of substituents also significantly affects the inhibitory potential of analogs, as demonstrated by this measurement, where *para*-Chloro (**17**) was found to be much more potent than *ortho* and *meta*. In this case, the chloro group is attached to a different position of an aromatic ring, which has a significant impact. The strong inhibitory potential of analogs might be the presence of halogen atom at *para*-position dominantly increases the ring charge which produces greater effects for inhibitions.

Similarly, hydroxyl group-containing analogs (**10**, **14**, and **16**) were found with excellent α -amylase and α -glucosidase inhibitory profiles. The creation of powerful hydrogen bonds with the active sites of enzymes may be the cause of the –OH-bearing analogs' inhibitory potentials. In this regard position and the number of the –OH group on the aromatic ring are also crucial for greater interactions therefore analog **14** ($IC_{50} = 0.70 \pm 0.50$ and $1.20 \pm 0.10 \mu\text{M}$) has two –OH groups at *meta*-position. The presence of one –OH **16**

($IC_{50} = 2.50 \pm 0.10$ and $3.50 \pm 0.10 \mu\text{M}$) activity profile was found lower and analog **10** ($IC_{50} = 1.30 \pm 0.10$ and $1.70 \pm 0.10 \mu\text{M}$) showed somewhat better activity than analog **16** might be the presence of two Chloro group on both *meta*-position of the ring. The activity profile of –OH analogs was found potent when comparing their biological potential to standard drug acarbose ($IC_{50} = 3.66 \pm 0.12$ and $4.85 \pm 0.11 \mu\text{M}$).

Methyl-substituted analogs (**2** and **8**) were also discovered to have an action similar to that of the medication acarbose. Here, in this comparison position of attached substituents also matters to the biological profile of the analog. The Methyl group attached to the aromatic ring at *para* and *ortho*-position respectively. The activity profile of the competitive analog was found better in the case of *para*-substituted analog **2** ($IC_{50} = 4.60 \pm 0.10$ and $5.90 \pm 0.10 \mu\text{M}$) than analog **8** ($IC_{50} = 5.30 \pm 0.20$ and $7.20 \pm 0.10 \mu\text{M}$).

3.1.1. The general structure of the molecule

The general structure represents the different parts of the molecule and varied substitutions attached to the aromatic ring. These substituents play a key role in the biological nature of molecules as discussed above. General representation of molecule as displayed in Fig. 2.

All of the screen compounds were discovered to have similar activity, however, certain analogs were discovered to have a few folds better results in both amylase and glucosidase than the conventional medication acarbose. Compounds **1**, **4**, **9**, and **14** had impressive potential in this respect, suggesting that the improved activity may be caused by the presence of connected functional groups, which improves ring activity for better interaction.

4. Molecular docking study

A molecular docking study was conducted for subjected (synthesized molecules having much potential against α -amylase and α -glucosidase) analogs which were found with excellent interactions in a superimposed complex. Analogues' potent binding abilities are caused by the functional group that is connected at a variety of positions on the aromatic ring. Grater hydrogen bonding was observed in the case of trifluoro, nitro and hydroxyl-containing moieties. Most of the analogs were found with good to poor interactions this may be the attached substituents but **1**, **4**, **9** and **14** were the most active analogs with the greater number of interactions (see Table 1).

The binding interaction of a molecule with an enzyme's active site is revealed by molecular docking research, which

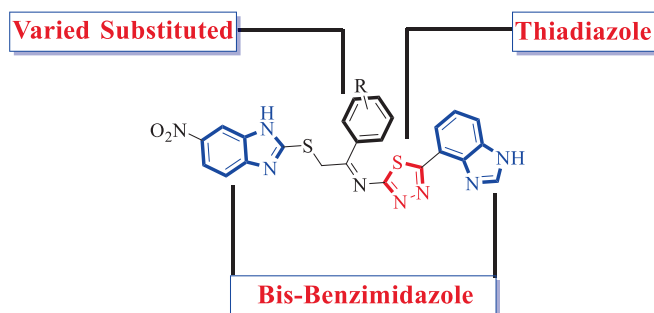
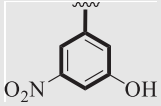

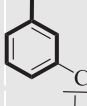
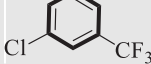
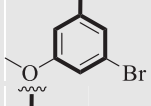
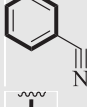
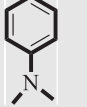
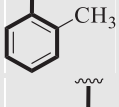
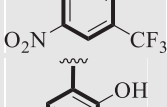
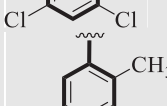
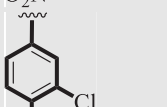
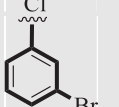
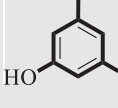



Fig. 2 General representation of the molecule.

Table 1 Bis-benzimidazole-based thiadiazole (1–18) derivatives and their α -amylase, α -glucosidase inhibitory profile.

S.NO	R	α -amylase inhibition IC ₅₀ (μ M)	α -glucosidase inhibition IC ₅₀ (μ M)
1		1.10 \pm 0.10	1.80 \pm 0.10
2		4.60 \pm 0.10	5.90 \pm 0.10
3		3.40 \pm 0.10	5.80 \pm 0.10
4		1.20 \pm 0.20	2.0 \pm 0.20
5		19.80 \pm 0.20	21.50 \pm 0.20
6		17.40 \pm 0.05	18.10 \pm 0.05
7		15.60 \pm 0.30	16.30 \pm 0.30
8		5.30 \pm 0.20	7.20 \pm 0.10
9		0.10 \pm 0.50	0.20 \pm 0.50
10		1.30 \pm 0.10	1.70 \pm 0.10
11		3.40 \pm 0.10	4.70 \pm 0.10
12		6.10 \pm 0.10	7.70 \pm 0.10
13		23.20 \pm 0.50	24.30 \pm 0.50
14		0.70 \pm 0.50	1.20 \pm 0.10

(continued on next page)

Table 1 (continued)


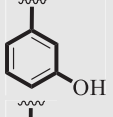


S.NO	R	α -amylase inhibition IC ₅₀ (μ M)	α -glucosidase inhibition IC ₅₀ (μ M)
15		6.10 \pm 0.10	8.30 \pm 0.10
16		2.50 \pm 0.10	3.50 \pm 0.10
17		2.80 \pm 0.10	3.70 \pm 0.10
18		22.70 \pm 0.20	23.70 \pm 0.10
Standard drug Acarbose		3.66 \pm 0.12	4.85 \pm 0.11

Table 2 Represent the binding interactions of the molecule with enzyme active residues.

Compound	Receptor	Interaction	Distance	Docking Score
Analog 1(A) against α -Amylase	TYR-A-334	Pi-Sulphur	4.54A $^\circ$	-12.9
	TYP-A-334	Pi-Pi-Stacked	4.50A $^\circ$	
	TRP-A-279	Pi-Pi-T-Shaped	5.76A $^\circ$	
	SER-A-286	Hydrogen-Bond	4.35A $^\circ$	
	GLY-A-117	Hydrogen-Bond	3.35A $^\circ$	
	TYR-A-116	Vander wall	6.86A $^\circ$	
	TRP-A-84	Pi-Pi Stacked	5.48A $^\circ$	
	PHE-A-330	Pi-Pi Stacked	4.58A $^\circ$	
	TYR-A-121	Hydrogen-Bond	7.74A $^\circ$	
	SER-A-81	Carbon-Hydrogen	3.54 A $^\circ$	
Analog 1(B) against α -Glucosidase	ALA-A-328	Pi-Alkyl	6.33A $^\circ$	-11.4
	TRP-A-82	Conventional H-B	5.13A $^\circ$	
	GLY-A-116	Pi-Pi Stacked	4.30A $^\circ$	
	HIS-A-438	Pi-Cation	6.19A $^\circ$	
	GLU-A-197	Pi. Hydrogen-Bond	6.14A $^\circ$	
	SER-A-287	Hydrogen-Bond	3.00A $^\circ$	
	ASP-A-70	Hydrogen-Bond	3.78A $^\circ$	
	TYR-A-332	Amide Pi-stacked	4.92A $^\circ$	
	SER-A-287	Hydrogen-Flouride	4.58A $^\circ$	
	SER-A-287	Hydrogen-Flouride	5.39A $^\circ$	
Analog 4(C) against α -Amylase	TYR-A-322	Hydrogen-Bond	5.78A $^\circ$	-11.7
	ASP-A-70	Conventional H-B	4.34A $^\circ$	
	PHE-A-329	Pi-Pi- T-shaped	5.22A $^\circ$	
	TRP-A-430	Vander wall	5.31A $^\circ$	
	TRP-A-440	Vander wall	5.96A $^\circ$	
	ALA-A328	Pi-Alkyl	5.25A $^\circ$	
	TRP-A-82	Conventional H-B	4.37A $^\circ$	
	GLU-A-197	Conventional H-B	4.19A $^\circ$	
	ASN-A-85	Hydrogen-Flouride	3.53A $^\circ$	
	TYR-A-84	Hydrogen-Flouride	6.17A $^\circ$	
Analog 4(D) against α -Glucosidase	TYR-A-70	Hydrogen-Flouride	6.71A $^\circ$	-12.5
	ASP-A-72	Pi-Anion	4.33A $^\circ$	

Table 2 (continued)

Compound	Receptor	Interaction	Distance	Docking Score		
Analog 9(E) against α -Amylase	TYR-A-121	Vander wall	7.13A°	-12.8		
	PHE-A-330	Pi-Pi T-shaped	4.58A°			
	TYR-A-130	Vander wall	6.85A°			
	GLY-A-117	Hydrogen-Bond	3.41A°			
	PHE-A-331	Pi-Pi T-shaped	5.65A°			
	TYR-A-334	Pi-Pi Sacked	4.57A°			
	TRP-A-279	Pi-Pi T-shaped	6.69A			
	TRP-A-334	Hydrogen-Flouride	4.95A°			
	TRP-A-279	Pi-Alkyl	5.82A°			
	TRP-A-334	Pi-Sulphur	4.11A°			
	TRP-A-121	Vander wall	5.77A°			
	ASP-A-72	Pi-Sulphur	4.35A°			
	GLY-A-123	Hydrogen-Bond	3.96A°			
	ASN-A-85	Carbon-Hydrogen bond	3.91A°			
PRO-A-86	Carbon-Hydrogen bond	4.46A°				
Analog 9(F) against α -Glucosidase	GLU-A-199	Pi-Anion	7.85A°	-12.3		
	GLY-A-118	Pi- Hydrogen-Bond	3.76A°			
	ARG-A-289	Conventional H-B	4.85A°			
	TRP-A-231	Pi-Alkyl	4.33A°			
	PHE-A-398	Pi-Alkyl	6.69A°			
	GLY-A-117	Carbon-Hydrogen bond	3.83A°			
	PHE-A-329	Pi-Pi-Stacked	6.88A°			
	HIS-A-438	Vander wall	5.11A°			
	SER-A-198	Conventional H-B	4.40A°			
	TYR-A-332	Pi-Pi T-shaped	5.48A°			
	TRP-A-82	Conventional H-B	5.13A°			
	TYR-A-440	Conventional H-B	5.54A°			
	ALA-A-328	Pi-Alkyl	6.39A°			
	ALA-A-277	Pi-Alkyl	4.18A°			
Analog 14 (G) against α -Amylase	TYR-A-130	Conventional H-B	6.75A°	-12.2		
	GLY-A-117	Hydrogen-Bond	3.36A°			
	PHE-A-330	Pi-Pi T-shaped	4.59A°			
	TRP-A-84	Carbon-Hydrogen bond	5.46A°			
	TYR-A-121	Conventional H-B	7.17A°			
	SER-A-81	Hydrogen-Bond	2.76A°			
	TYR-A-334	Pi-Pi Stacked	4.64A°			
	TRP-A-279	Pi-Pi T-shaped	5.76A°			
	PHE-A-331	Carbon-Hydrogen bond	4.51A°			
	SER-A-286	Conventional H-B	4.23A°			
	TYR-A-128	Conventional H-B	6.06A°			
	TRP-A-82	Pi-Pi T-shaped	4.19A°			
	TRP-A-82	Pi-Pi T-shaped	6.17A°			
	GLY-A-117	Hydrogen-Bond	3.50A°			
Analog 14 (H) against α -Glucosidase	SER-A-198	Carbon-Hydrogen bond	4.16A°	-11.5		
	PHE-A-329	Pi-Pi Stacked	5.94A°			
	PRO-A-285	Conventional H-B	6.06A°			
	ASP-A-70	Pi-Anion	3.90A°			
	ASP-A-300	Conventional H-B	4.69A°			
	ASP-A-300	Conventional H-B	4.94A°			
	GLU-A-233	Conventional H-B	4.62A°			
	GLU-A-233	Conventional H-B	4.63A°			
	HIS-A-201	Carbon H-B	4.63A°			
	GLU-A-240	Conventional H-B	5.50A°			
	Acarbose in α -amylase complex	ASP-A-232	Conventional H-B		4.50A°	-70.5
		LYS-A-506	Conventional H-B		3.71A°	
		ASN-A-496	Conventional H-B		4.81A°	
		SER-A-505	Conventional H-B		3.72A°	
GLU-A-603		Conventional H-B	4.08A°			
ALA-A-232		Carbon H-B	5.29A°			
Acarbose in α -glucosidase				-91.5		

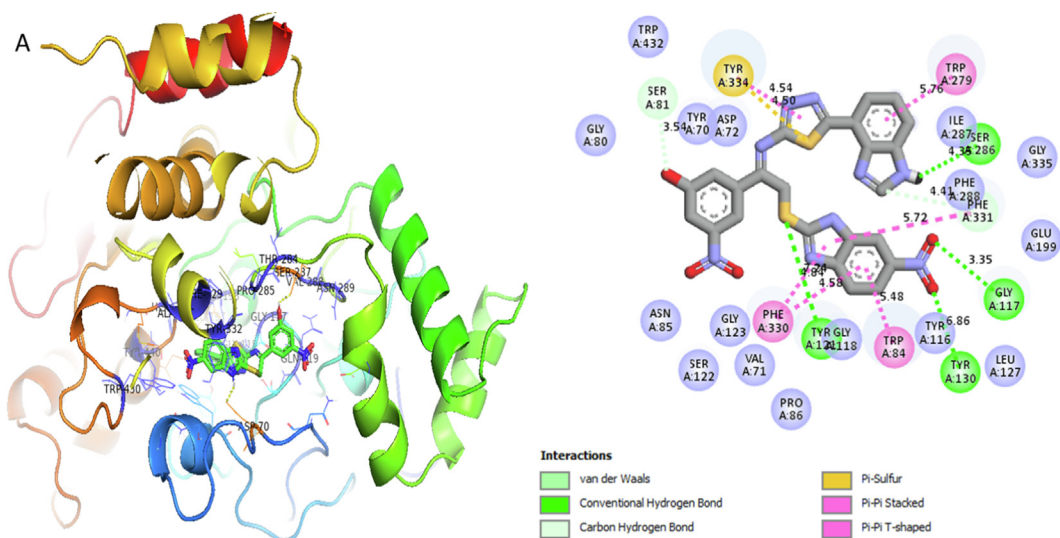


Fig. 3 Represent 2D and 3D structure for analogue1-A in α -amylase complex.

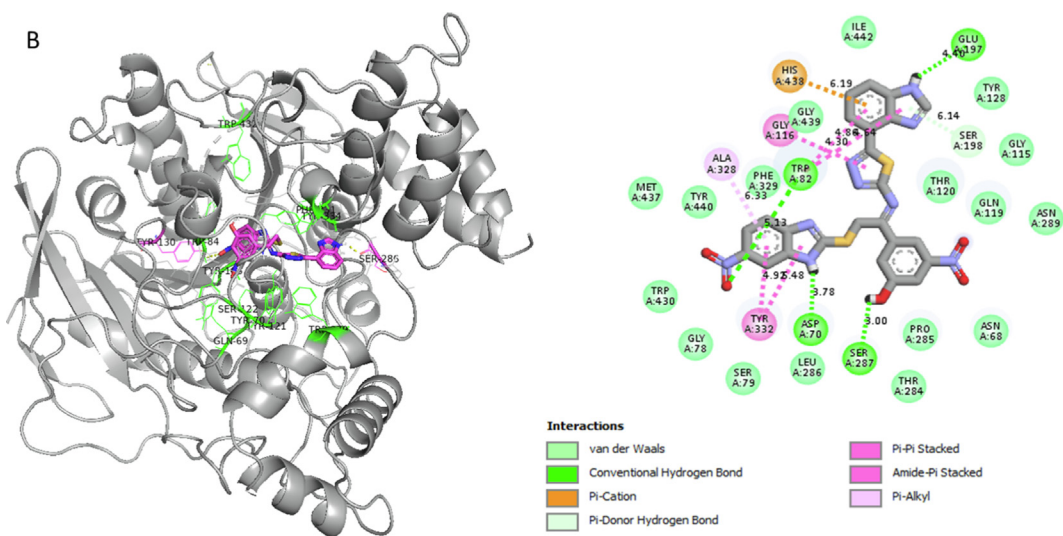


Fig. 4 Represent 2D and 3D structure for analogue1-B in α -glucosidase complex.

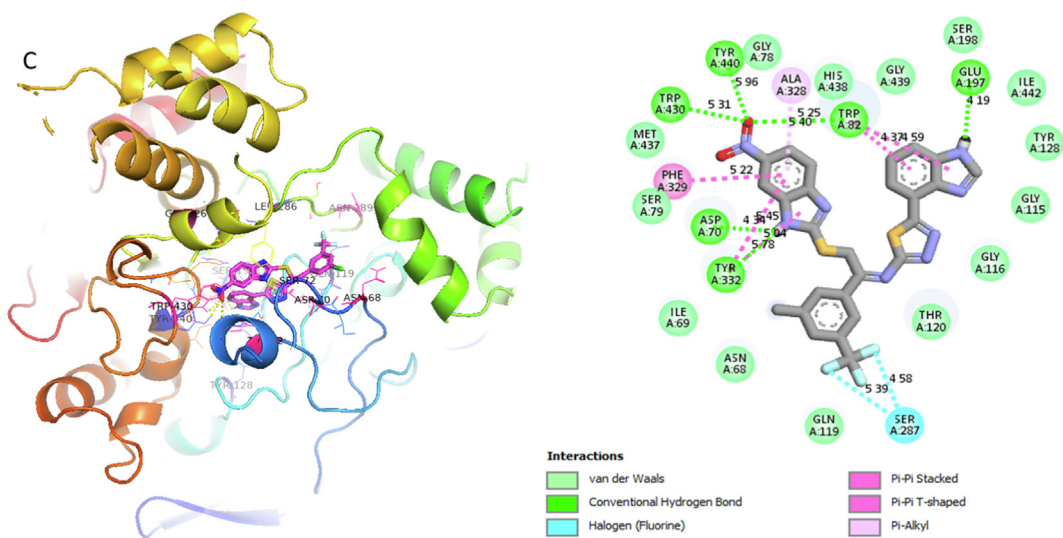


Fig. 5 Represent 2D and 3D structure for analog 4-C in α -amylase complex.

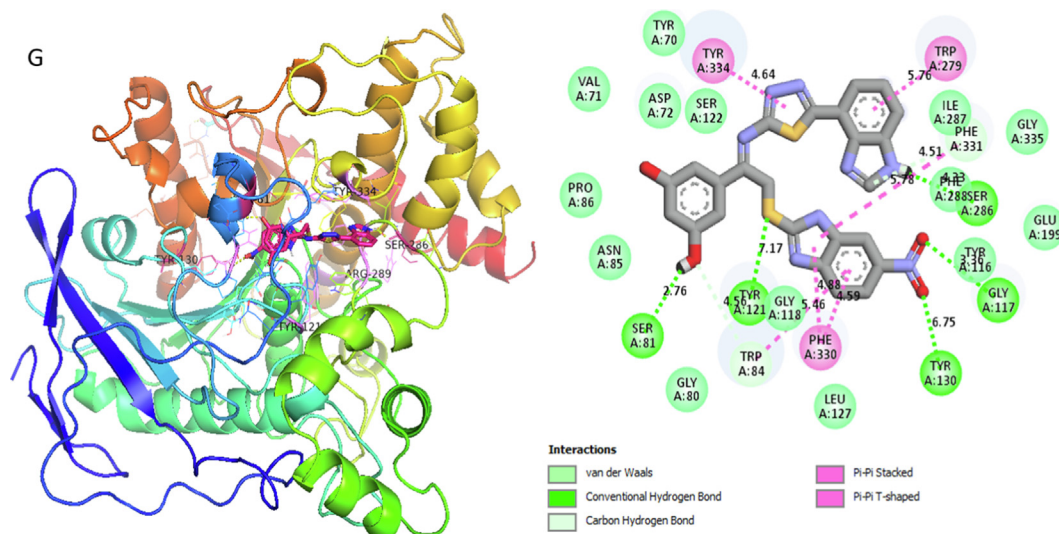


Fig. 9 Represent 2D and 3D structure for analog 14-G in α -amylase complex.

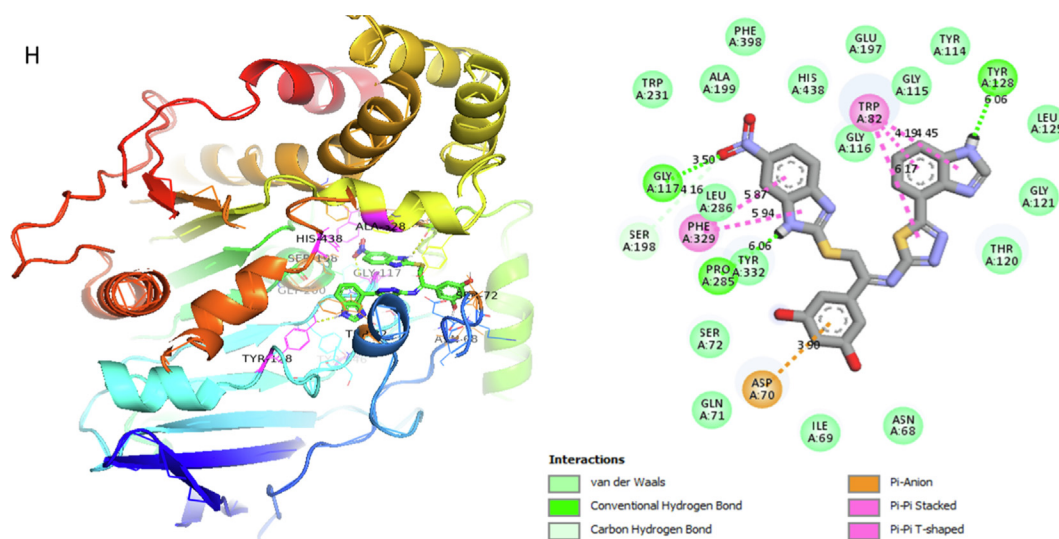


Fig. 10 Represent 2D and 3D structure for analog 14-H in α -glucosidase complex.

depends on the kind of attached substituents and how they affect the interactive features. Molecular docking was performed by using varied software such as Auto dock vina (1.5.7), Molecular operational environment (MOE-2015) and discovery studio visualizer (DSV-2021) (Kharb et al., 2012; Khan et al., 2022; Li et al., 2015; Rao et al., 2021; Khan et al., 2022; Khan et al., 2022). Molecular docking studies were performed in three steps, in the first step both protein (retrieved from RCSB protein data bank by thorough codes 1b2y and 3w37 for α -amylase and α -glucosidase respectively) and ligand were prepared and energy was minimized in MOE. In the next step, both protein and ligand were transferred to the auto dock where water was removed and polar hydrogen, as well as Kollman and Gasteiger charges, were added. After completion, the protein, ligand and their X, Y

and Z coordinate were saved in PDBQT and text format respectively. In the last step, the location of the docking folder was set and using command prompt to carry out the molecular docking study. Finally, DSV was used to explore the binding interaction (Table 2) in the form of 2D and 3D structures as shown in Figs. 3-10.

Docking score were calculated for analogs **1**, **4**, **9** and **14** due to varied functionalities and position produced different affect which also increase or decrease the binding interaction therefore their docking score is different from one another and their interactions ranges also. The potency of these compounds might be the presence of functional group, position and number of substituents which enhance or reduce the binding interactions of molecules in a complex (Table 2) (see Fig. 11).

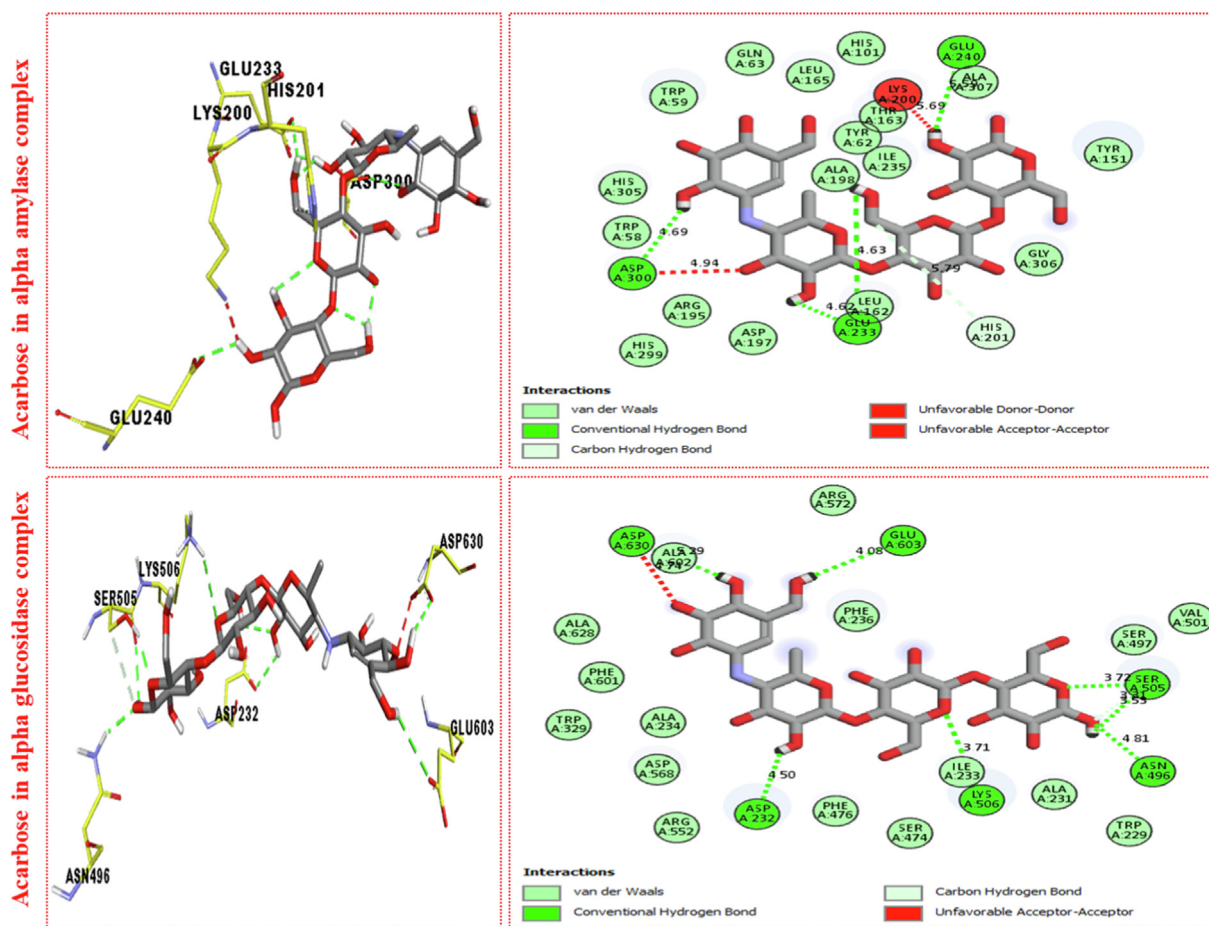
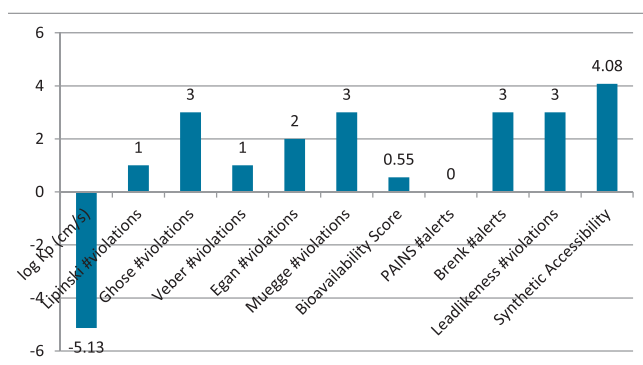
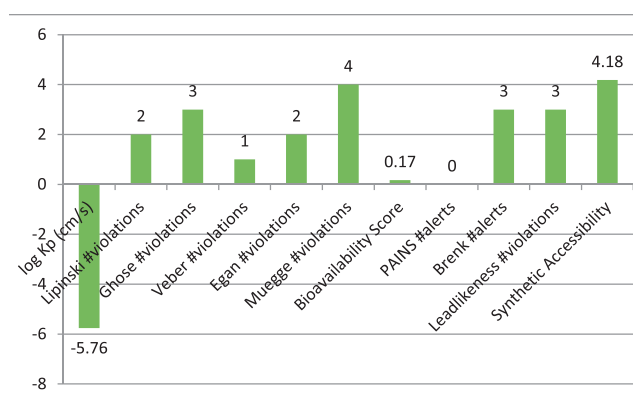


Fig. 11 Represent 2D and 3D structure for acarbose in both α -amylase and α -glucosidase complex.



Graph 1 Show compound-1's ADMET characteristics.



Graph 2 Describe compound-4's ADMET characteristics.

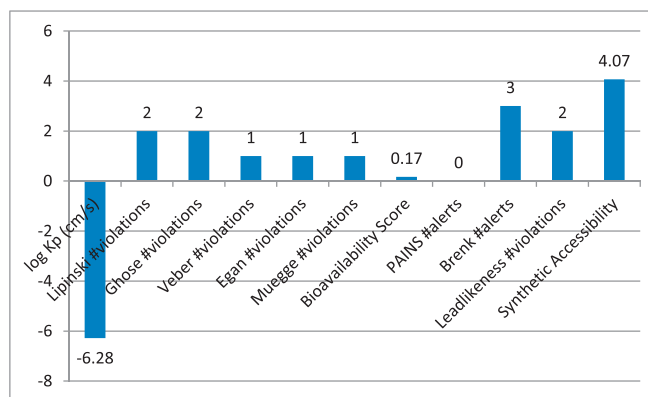
5. ADMET prediction

Through the use of the online tool SwissADME, several features of the compounds used in this research were identified to assure absorption, distribution, metabolism, excretion, and toxicity. This research observed the log Kp, Ghose, Veber, Lipinski, Muegge violations, gan, PAINS, Brenk alerts, Bioavailability score, as well as Leadlikeness violations. The findings for the tested candidates 1, 4, 9 and 14 were

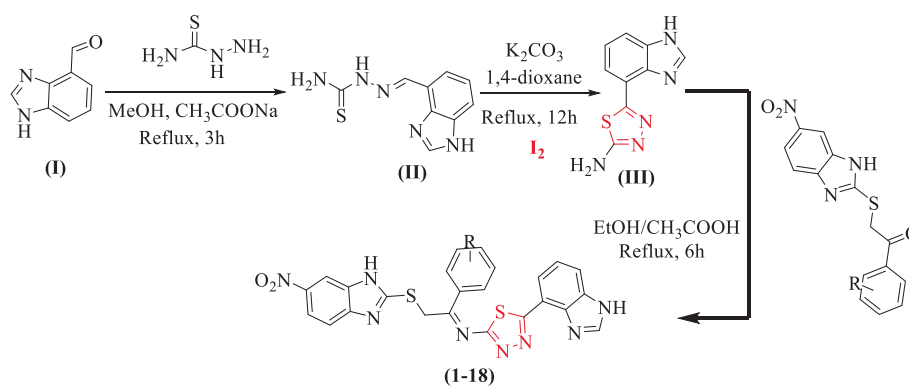
significant, as shown in Graph 1-4. The characteristics of the examined substances showed a definite difference.

6. Conclusion

A series of processes were used to create the bis-benzothiazole-based thiadiazole analogs (1–18), and these reactions were verified by employing spectroscopic methods such as ¹H NMR, ¹³C NMR,



Graph 3 Represent the ADMET properties of compound-9.



Graph 4 Represent the ADMET properties of compound-14.

and HREI-MS. All of the produced analogs were also tested against the enzymes glucosidase and amylase. When compared to the standard medication acarbose, the derivatives 1, 4, 9, and 14 were found to have excellent activities against both -amylase and -glucosidase. The majority of them, which had various substituents at various positions of the aromatic ring, displayed good to moderate inhibitory activity. An analysis of the topic analogs' major binding modes using molecular docking technology was also found. As well as ADMET study also revealed the varied significant properties of the selected compounds. Among the evaluated (E)-N-(5-(1H-benzo[d]imidazol-4-yl)-1,3,4-thiadiazol-2-yl)-2-((6-nitro-1H-benzo[d]imidazol-2-yl)thio)-1-(3-nitro-5-(trifluoromethyl)phenyl)ethan-1-imine **9** ($\text{IC}_{50} = 0.10 \pm 0.050$ and $0.20 \pm 0.05 \mu\text{M}$ respectively) was considered as the most potent one. Inhibitors of -amylase and -glucosidase are found in a novel family of thiadiazole compounds based on bis-benzimidazoles in this investigation.

Author contributions

The manuscript was written with the contributions of all authors. All authors have approved the final version of the manuscript.

Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.arabjc.2023.104847>.

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