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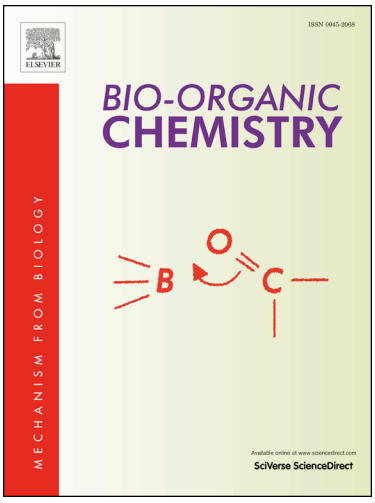

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Synthesis, α-Glucosidase Inhibitory Potential, *In Vitro,* and *In Silico* Studies on 5-Chloro-2-Aryl Benzo[*d*]thiazoles

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Abstract: Twenty-five derivatives of 5-chloro-2-aryl benzo[d]thiazole (**1-25**) were synthesized and evaluated for their α-glucosidase inhibitory activity *in vitro*. Among them eight compounds showed potent activity with IC_{50} values between 22.1 ± 0.9 to 136.2 ± 5.7 μM, when compared with standard acarbose (IC_{50} = 840 ± 1.7 μM). The most potent compounds **4**, **9**, and **10** showed IC_{50} values within the range of 22.1 ± 0.9 to 25.6 ± 1.5 μM. Compounds **2**, **5**, **11**, and **19** showed IC_{50} values within the range of 40.2 ± 0.5 to 60.9 ± 2.0 μM. Compounds **1** and **3** were also found to be good inhibitors with IC_{50} values 136.2 ±5.7 and 104.8 ± 9.9 μM, respectively. The remaining compounds were inactive. Structure-activity relationships (SAR) have also been established. Kinetics studies indicated compounds **2**, **3**, **10**, **19**, and **25** to be non-competitive, while **1**, **5**, **9**, and **11** as competitive inhibitors of α-glucosidase enzyme. Furthermore, molecular interactions of active compounds with the enzyme binding sites were predicted through molecular modelling studies.

Keywords: 5-Chloro-2-aryl benzo[d]thiazole; α-glucosidase; diabetes mellitus; hyperglycemia; *in silico* studies.

1 Introduction

α-Glucosidase inhibitors are antidiabetic drugs used for the prevention of post-prandial hyperglycemia in type-II diabetes [1]. Diabetes mellitus type II is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance, and relative insulin deficiency. The classic symptoms are excessive thirst, frequent urination, and constant hunger. Obesity is now recognized as the primary cause of type II diabetes in people who are genetically predisposed to the disease [2]. α-Glucosidase inhibitors are used to maintain high glycemic control along with other insulin secretagogues [3].

Absolute or relative deficiency in insulin secretions and/or insulin resistance results in hypoglycaemia, which is associated with diabetes mellitus [4]. It is estimated that by the year of 2025 diabetes mellitus will affect 300 million people worldwide [5], thus there is an urgent need to develop improved therapies for this chronic disorder. One of the approaches to manage this disease is to control the activity of α-glucosidase (EC.3.2.1.20), which is an enzyme positioned at small intestine. This enzyme is responsible for the cleavage of α-1-4 bond linkage in starch or oligosaccharides into monosaccharides such as glucose [6]. Therefore, inhibition of α-glucosidase can help in the post-prandial hyperglycemia, and associated complications.

Benzothiazole is a class of heterocyclic compounds containing nitrogen and sulphur as heteroatoms. Structurally, benzothiazole skeleton is a fusion of benzene ring and thiazole moiety. They are pharmacologically active compounds with a wide spectrum of activities, such as anti-tuberculosis [7], anti-tumor [8], anti-cancer [9], antiviral [10], analgesic [11], LTD4 receptor antagonist [11] anticonvulsant [12], and antifungal [13]. Benzothiazoles also have importance in the field of polymer chemistry [14], medicines [15], and dyes [16, 17].

As discussed earlier, diabetes is a rapidly spreading disease, and its prevalence increases day by day. Benzothiazole nucleus has the ability to control diabetes mellitus. Since, it is involved in inhibition of 11-hydroxysteroid dehydrogenase type 1 [18], it has the ability to stimulate insulin secretion [19] and has known hypoglycaemic mechanism [20], *etc*.

Rationale of the current study:

Previously, our research group reported *in vitro* activity of benzothiazole Schiff bases against α-glucosidase enzyme [21] (Figure-1). In continuation of our studies on benzothiazole derivatives, we synthesized some new analogues, and evaluated their α-glucosidase activity. Compounds **1**, **3**, **4**, **8**, **9**, **13**, **18**, **19**, **21**, and **25** were identified as new while remaining compounds have been reported previously [22-28].

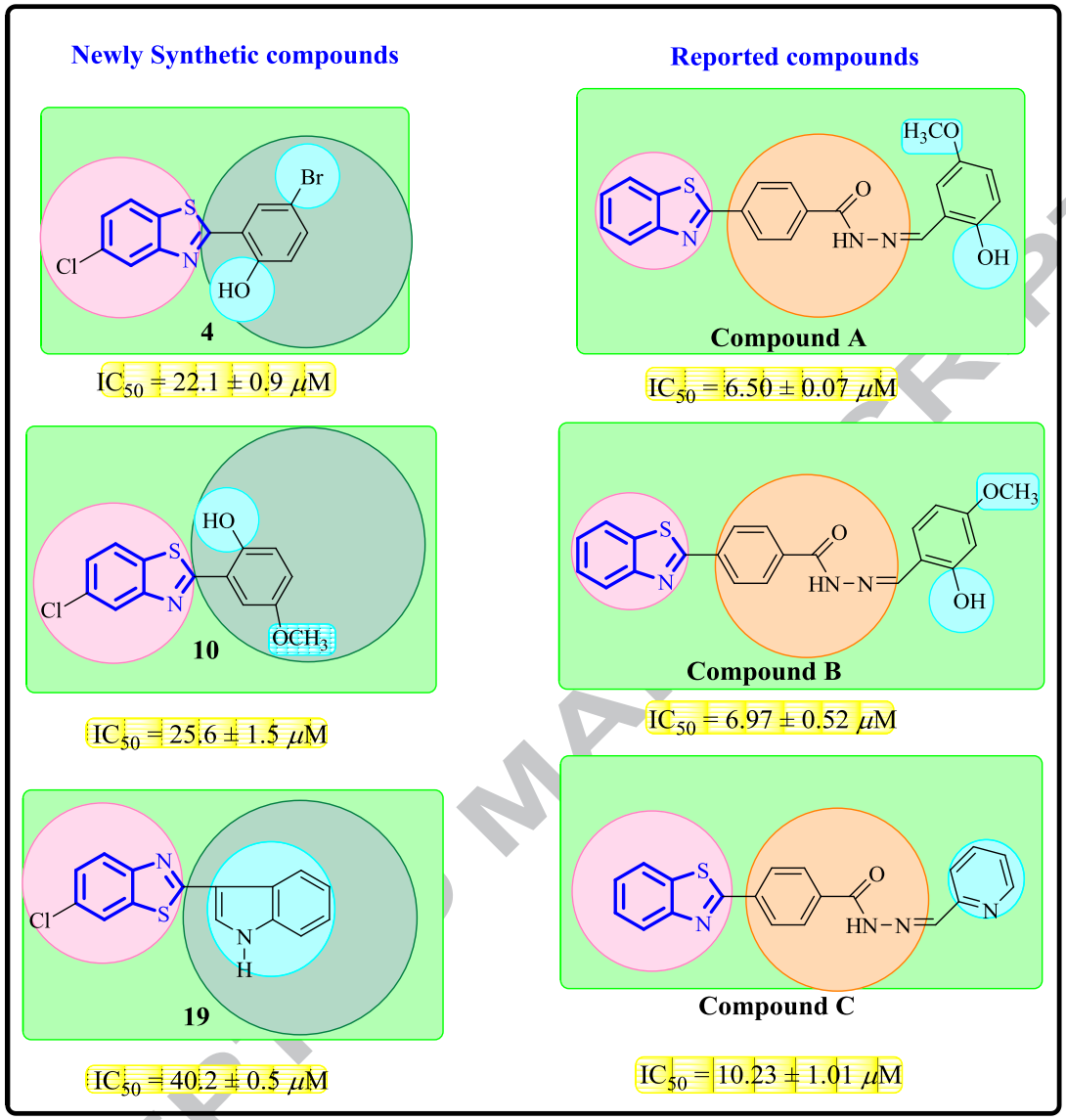


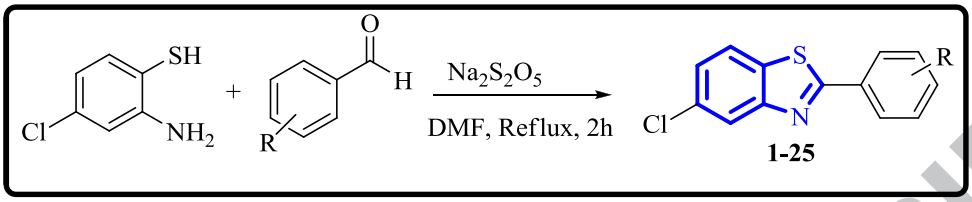
Figure-1: Rationale of Current Study.

2 Results and discussion

2.1 Chemistry

A library of 5-chloro-2-substituted benzothiazoles (**1-25**) were synthesized by reacting 4-chloro-2-aminothiophenol with different aromatic aldehydes in the presence of sodium metabisulfite ($Na_2S_2O_5$) in *N*,*N*-dimethylformamide (DMF) under reflux for 2 h. The mixture was cooled at room temperature, and poured on to cold water for precipitation. Filtration of precipitate, followed by washing with cool water resulted in pure benzothiazoles (**1-25**) (Scheme-1). Structures of the

synthetic compounds were identified by spectroscopic techniques, such as ^{1}H-NMR and EI-MS, and HREI-MS.

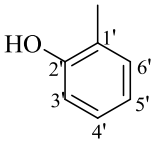
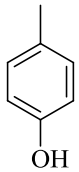


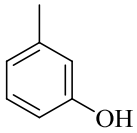
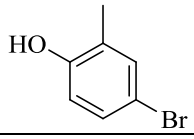
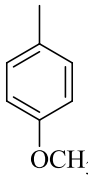
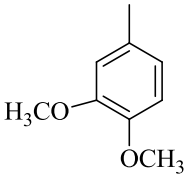
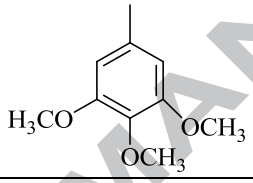
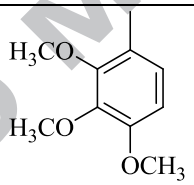
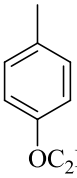
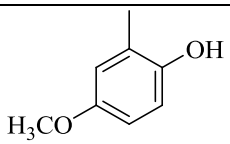
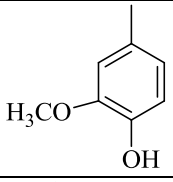
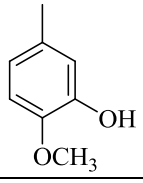
Schemes-1: Synthesis of 5-Chloro-2-aryl benzo[d]thiazole Derivatives.

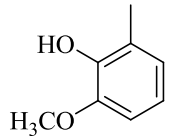
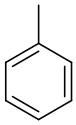
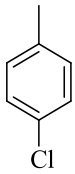
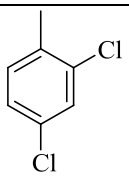
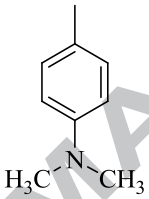
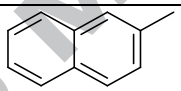
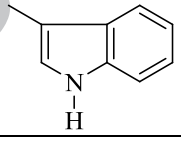
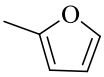
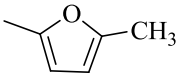
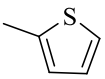
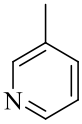
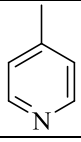
2.3 *α*-Glucosidase inhibition Studies

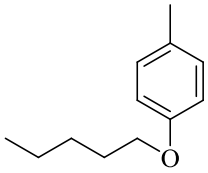
All synthetic 5-chloro-2-aryl benzo[d]thiazole (**1-25**) were evaluated for their *in vitro* *α*-glucosidase inhibitory activity. Among them, eight compounds showed potent activity, with IC_{50} values between 22.1 ± 0.9 to 136.2 ± 5.7 μM, as compared to standard acarbose (IC_{50} = 840 ± 1.7 μM) (Table-1). Compounds **4** (IC_{50} = 22.1 ± 0.9 μM), **9** (IC_{50} = 24.8 ± 0.4 μM), and **10** (IC_{50} = 25. 6± 1.5 μM) were found to be the most potent inhibitors in the series. Compounds **2**, **5**, **11**, and **19** also showed prominent IC_{50} values within the range of 40.2 ± 0.5 to 60.9 ± 2.0 μM. Compound **1** (IC_{50} = 136.2 ±5.7 μM) and **3** (IC_{50} = 104.8 ± 9.9 μM) were also found to be good inhibitors of *α*-glucosidase. Remaining compounds were found to be inactive. To study the substituent effects on benzothiazoe moiety with respect to *α*-glucosidase inhibitory activity a structure-activity relationship (SAR) has also been established. Furthermore, molecular interactions of active compounds with the enzyme binding sites were predicted through molecular modelling studies.

Table-1: *α*-Glucosidase inhibitory activity of 5-chloro-2-aryl benzo[d]thiazole derivatives 1-25.

Compounds	Aryl part	IC_{50} ± SEM[a] [μM]
1		136.2 ± 5.7
2		60.9 ± 2.0

3		104.8 ± 9.9
4		22.1 ± 0.9
5		53.4 ± 4.3
6		N.A.[b]
7		N.A.[b]
8		N.A.[b]
9		24.8 ± 0.4
10		25. 6± 1.5
11		52.7 ± 1.0
12		N.A.[b]

13		N.A.[b]
14		N.A.[b]
15		N.A.[b]
16		N.A.[b]
17		N.A.[b]
18		N.A.[b]
19		40.2 ± 0.5
20		N.A.[b]
21		N.A.[b]
22		N.A.[b]
23		N.A.[b]
24		N.A.[b]

25		180 ± 1.25

SEM[a] means Standard Error of the Mean; N.A.[b] means Not Active; Standard: Acarbose, IC_{50} ± SEM = 840 ± 1.73 μM.

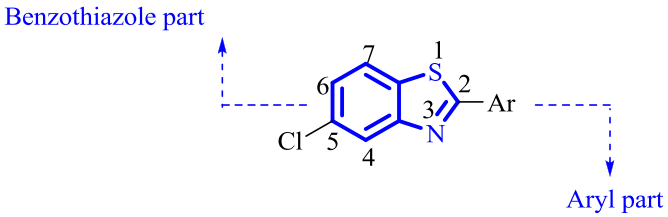


Figure-2: 5-Chloro-2-aryl benzo[d]thiazole

Structure-activity relationship (SAR) studies of twenty-five derivatives of 5-chloro-2-aryl benzo[*d*]thiazole towards α-glucosidase inhibition indicates that different substituents at the aryl part of 5-chloro-2-aryl benzo[*d*]thiazole are responsible for their varying degree of activities. We have hypothetically divided the 5-chloro-2-aryl benzo[*d*]thiazole molecule in two parts (benzothiazole and aryl part) for better understanding the SAR (Figure-2).

Among the synthetic compounds, compound **4**, having hydroxyl at C-2' and bromo groups at C-5' positions, was found to be the most active member of the series (IC_{50} = 22.1 ± 0.92 μM), which is thirty-folds more active than the standard drug acarbose (IC_{50} = 840 ± 1.73 μM). Compound **1** having only hydroxyl group at C-2', showed a decreased activity (IC_{50} = 136.2 ± 5.7 μM); however, compound **2** (IC_{50} value of 60.9 ± 2.07 μM), having a hydroxyl group at C-4', showed an increased activity. Substituting the hydroxyl group at C-3' position resulted in decreased activity, as in compound **3 (**IC_{50} = 104.8 ± 9.92 μM) (Figure-3).

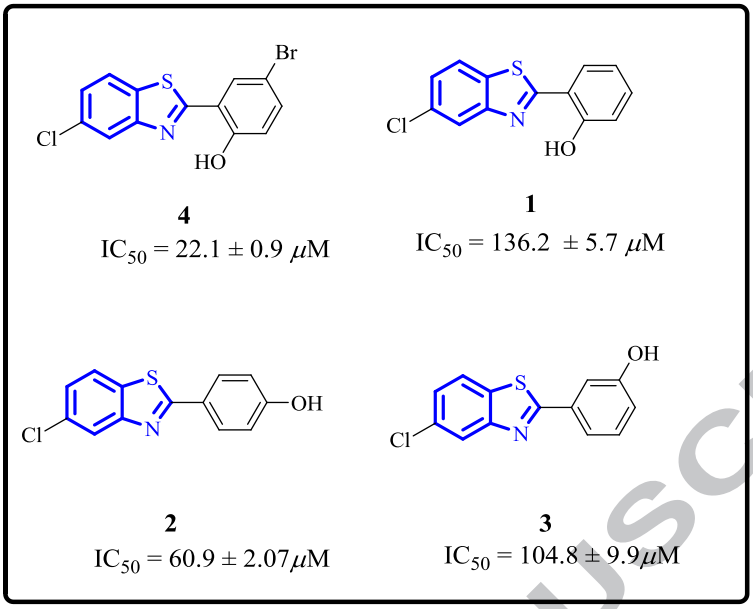


Figure-3: SAR of Hydroxyl and Bromo Substituted Aryl Part.

Interestingly, compound **10** with a hydroxyl at C-2' and a methoxy at C-5', displayed a good activity with an IC_{50} value of 25.6 ± 1.50 μM, while, compound **11** with a hydroxyl group at C-4' and methoxy group at C-5', displayed a decreased activity (IC_{50} = 52.7 ± 1.07 μM). Other combinations of hydroxyl and methoxy substituents (compounds **12** and **13**) were found to be inactive (Figure-4).

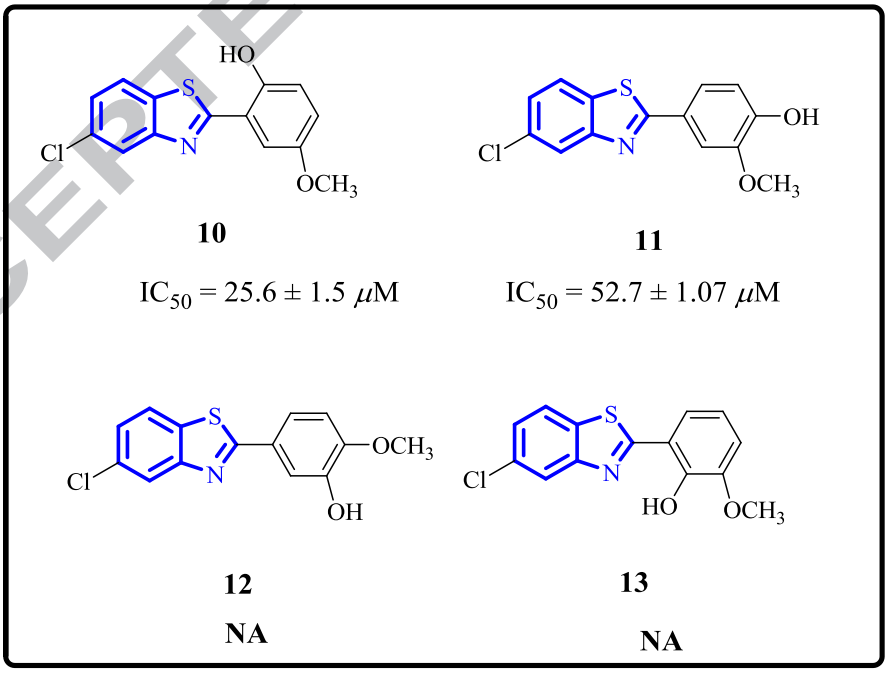


Figure-4: SAR of Hydroxyl And Methoxy Substituted Aryl Part.

Substitution of ethoxy group at C-4', as in compound **9,** resulted in a good inhibitory activity, with an IC_{50} value of 24.8 ± 0.40 μM. Amongst the compounds having only methoxy group at the phenyl moiety, compound **5** which has one methoxy substituent at C-4' was found to be active (IC_{50} = 53.4 ± 4.3 μM), whereas compounds **6**, **7**, and **8** each with two or three methoxy groups on the phenyl ring, were found to be inactive (Figure-5). Compound **25,** with phenoxy pentyl group, was found to be moderately active with IC_{50} value of 180 ± 1.25 μM.

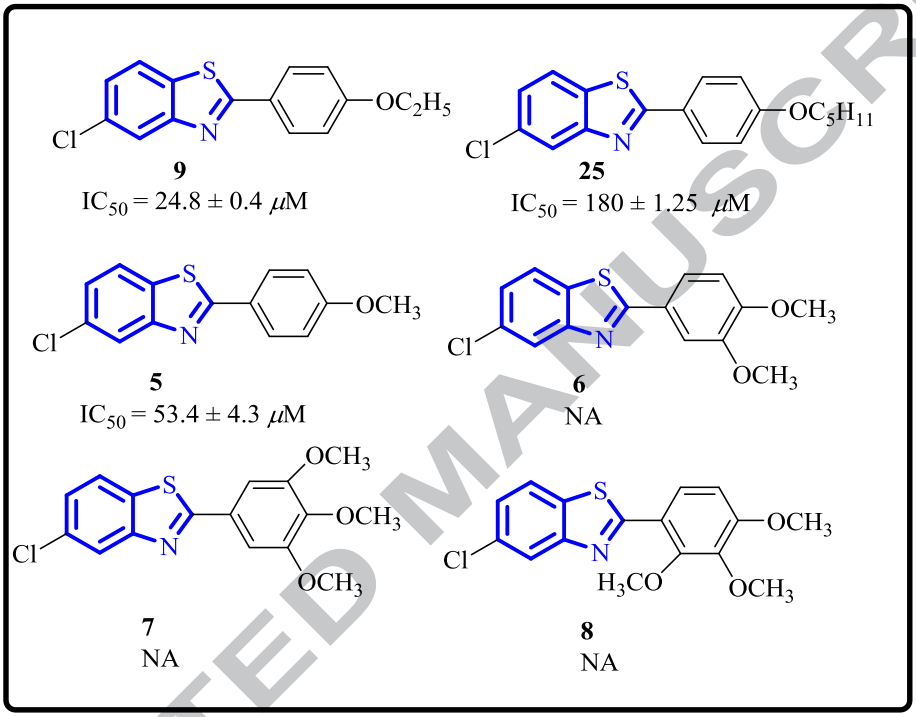


Figure-5: SAR of Alkoxy Substituted Aryl Part.

Good activity was observed when phenyl group was replaced with indole moiety, as in compound **19**, which displayed an IC_{50} value of 40.2 ± 0.5 μM (Figure-6).

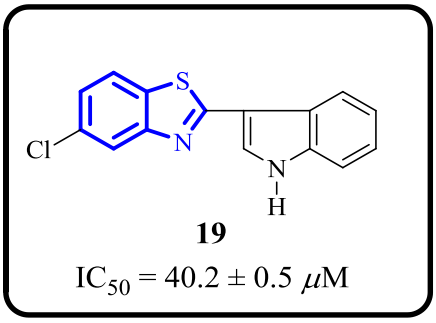


Figure-6: SAR of hetero-atomic substituted aryl part

Compounds **15**-**18**, and **20**-**24** were found to be completely inactive.

2.4 Kinetic studies

Active compounds of 5-chloro-2-arylbenzo[d]thiazole series (*i.e.* **1-5**, **9-11**, **19**, and **25**) were analyzed for kinetic studies (Figure-7, and 8). Among them, compounds **2**, **3**, **10**, **19**, and **25** were found to be non-competitive inhibitors of α-glucosidase, as these derivatives were able to decrease the *V*max, while *K*m remained unaffected. Compounds **1**, **5**, **9**, and **11 increased** the *K*m values while *V*max remains unaffected, hence considered as competitive inhibitor of the α -glucosidase enzyme(Table-2).

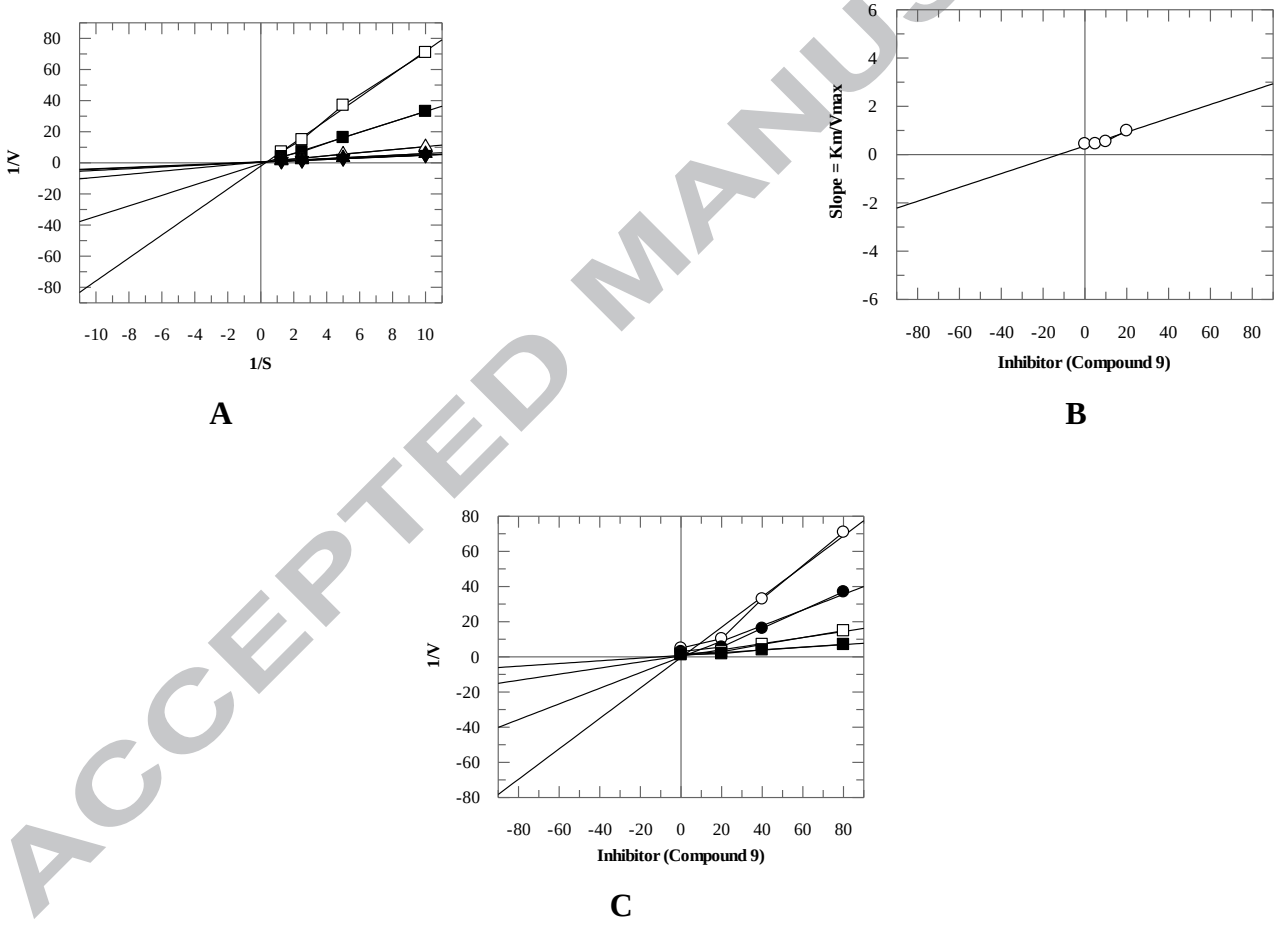


Figure-7: The mode of inhibition of *α*-glucosidase by compound 9, (A) Lineweaver-Burk plot of reciprocal rate of reaction (velocities) *vs* reciprocal of substrate in the absence (▽), and in the presence of 80 *μ*M (□), 40 *μ*M (■), 20 *μ*M (Δ), 10 *μ*M (▲), and 5 *μ*M (▼) of 9. (B) Secondary replot of Lineweaver-Burk plot between the slopes of each line on Lineweaver-Burk plot *vs* different concentrations of 9, and (C) Dixon plot of reciprocal rate of reaction (velocities) *vs* different concentrations of 9.

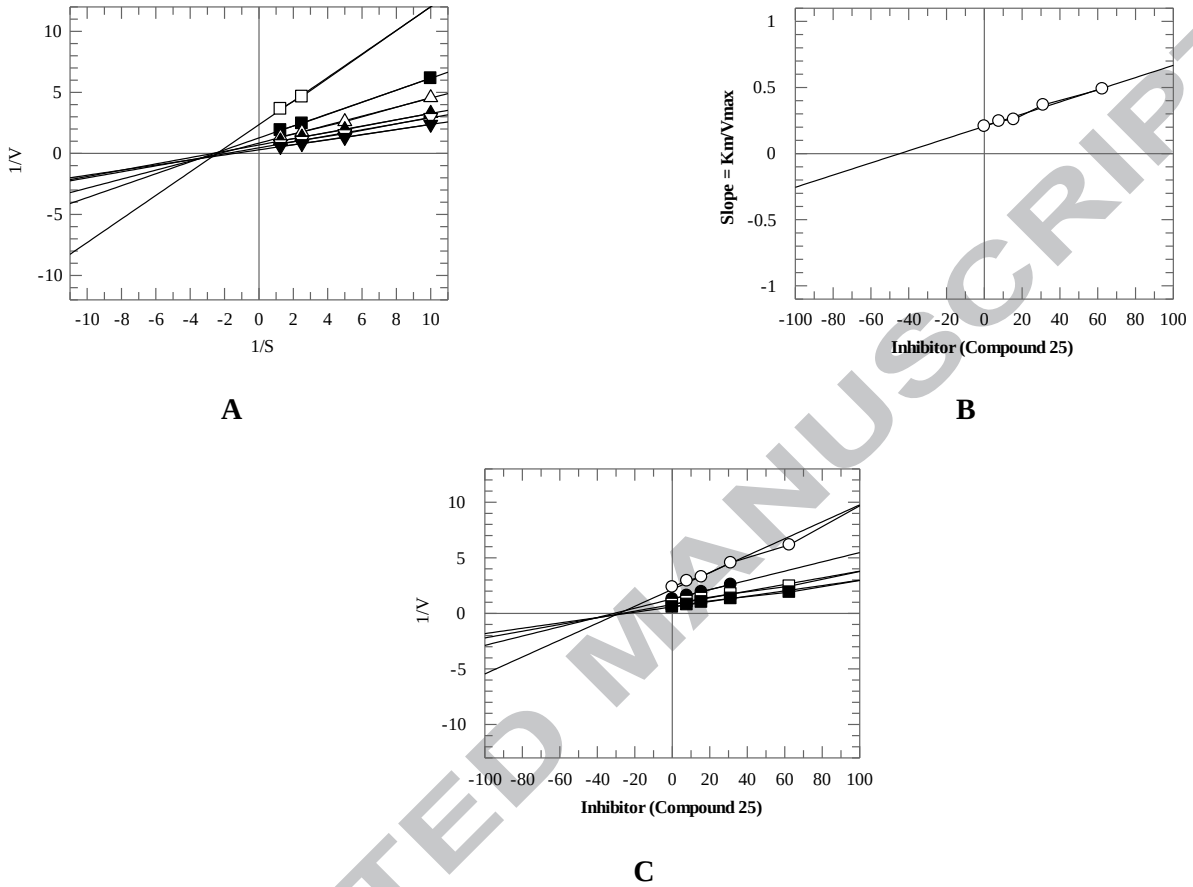


Figure-8: The mode of inhibition of *α*-glucosidase by compound 25, (A) Lineweaver-Burk plot of reciprocal rate of reaction (velocities) *vs* reciprocal of substrate in the absence (▼), and in the presence of 125 *μ*M (□), 62.5 *μ*M (■), 31.25 *μ*M (Δ), 15.625 *μ*M (▲), and 7.8125 *μ*M (▽) of 25. (B) Secondary replot of Lineweaver-Burk plot between the slopes of each line on Lineweaver-Burk plot *vs* different concentrations of 25, and (C) Dixon plot of reciprocal rate of reaction (velocities) *vs* different concentrations of 25.

Table-2: Kinetic studies of active compounds.

Compounds	*Ki* ± SEM[a] [*μ*M]	Type of Inhibition
1	14.1 ± 0.100	Competitive
2	25.8 ± 0.006	Non-competitive
3	26.6 ± 0.0001	Non-competitive
4	16.03 ± 0.0411	Non-competitive
5	25.5 ± 0.115	Competitive

9	12.39 ± 0.04	Competitive
10	5.70 ± 0.021	Non-competitive
11	59.75 ± 0.005	Competitive
19	10.55 ± .00017	Non-competitive
25	44.78 ± 0.005	Non-competitive

2.5 Computational modeling studies

Molecular modeling studies were carried out in order to investigate the binding mode of active compounds against α-glucosidase. In this connection, a homology model of the α-glucosidase (*S. cerevisae*) was developed, and the active compounds of the series were docked using Glide software [29].

Yeast α-glucosidase (EC 3.2.1.20) has been widely used to screen bioactive compounds targeting α-glucosidase. The lack of crystal structure was compensated using homology model developed using Yeast isomaltase (PDB 3AJ7) from the same specie [30], which was further refined using Prime. The quality of model was assessed using the Ramachandran plot which is a gold standard for the assessment of three-dimensional structures of protein [31]. A brief review of the plot shows that most of the residues lie in favored regions (92.2%) with only two outliers (Figure S1).

Molecular docking studies of selected compounds were carried out to elaborate the observed α-glucosidase inhibitory activity of the newly synthesized compounds. In order to challenge the ability of Glide to reproduce the crystal pose control docking experiments were carried out using PDBs 3A4A [32], and 3W37 [33]. The complex 3W37 represents the coordinates of Sugar Beet α-glucosidase and acarbose. While, the coordinates of the native ligand α-D-glucose in the active site of isomaltase are deposited as PDB 3A4A. The RMSD values between the crystal pose and docked poses in both cases was found to be less than 2 Å (Figure S2). The results of control docking validate the predictive ability of Glide to establish the binding mode of the inhibitors in the active site of the target enzyme.

Molecular docking studies of the newly synthesized benzothiazole derivatives **1**-**5**, **9**-**10**, **19**, and **25** was carried out using already validated protocol. The active site of the α-glucosidase is part of a larger pocket that is virtually separated by Phe157 and Phe300. The analysis of kinetic profile of the compounds suggests that the ligand binds in the close proximity of the substrate, thus variation in the position of the same moiety results in different inhibitory profile. Among the hydroxl substituted

derivatives (**1**-**4**), compound **4** bearing the hydroxyl and bromide substitution at C-2' and C-5' is the most active member of the series. The top ranked docked pose of the compound **4** is presented in Figure-9(a). The benzothiazole ring of the compound anchors the binding site by hydrophobic interactions with His279 and Glu304. The hydroxl moiety is involved in hydrogen bonding with the Arg312, in the active site of the protein. As mentioned earlier in the SAR analysis, the introduction of Bromide at with the C-5' position significantly increased the observed α-glucosidase inhibitory potential. The docking study suggests that the bromide moiety depicts halogen bond with Lys155. We hypothesize that the halogen interaction unique to compound **4** among the hydroxl derivatives is responsible for its activity.

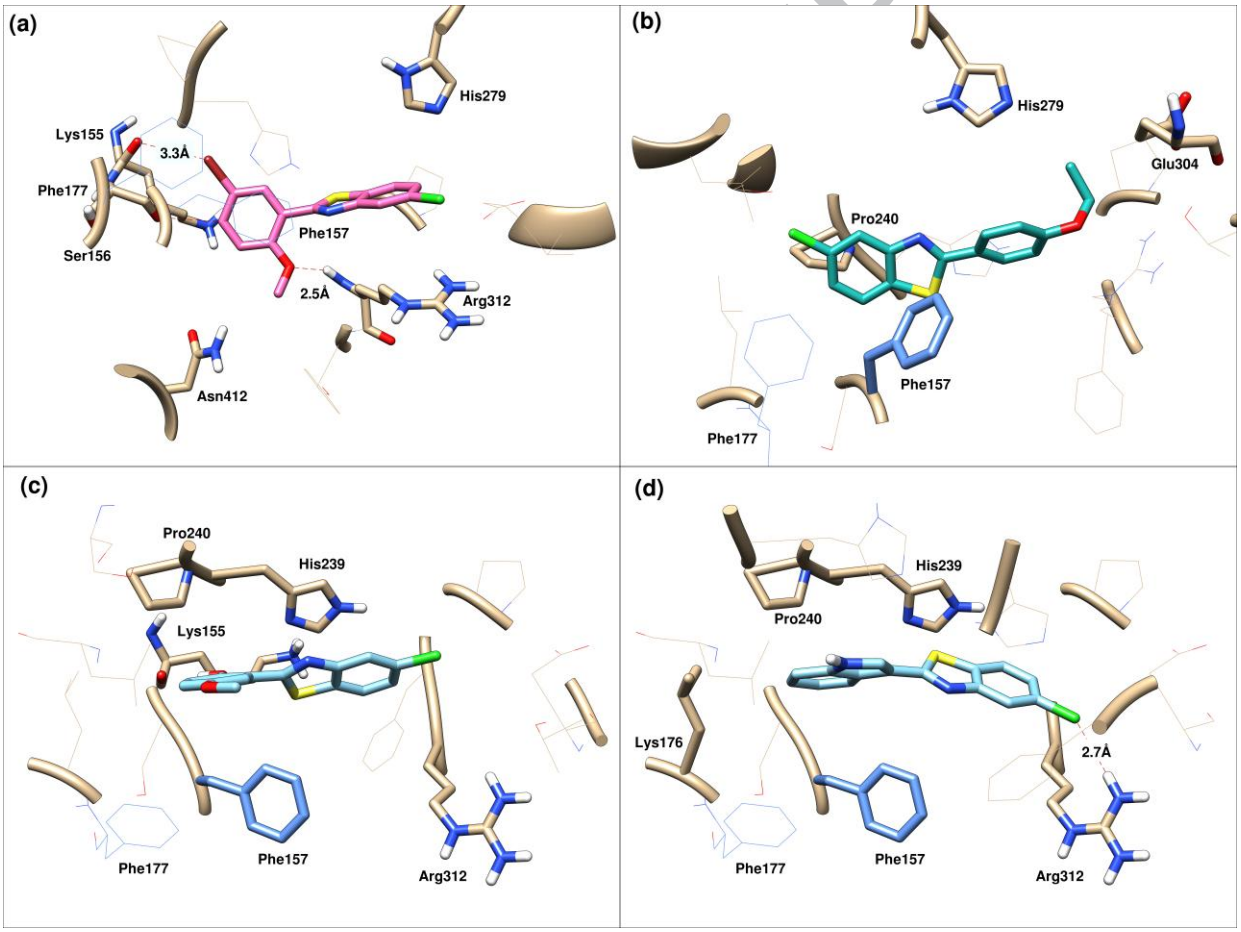


Figure-9: The top ranked docking pose of the compounds 4,9,10,19. The binding site is presented as tan wires and sticks, in case of native contacts and interactions, respectively. The panel (a) presents the docking pose of compound 4, (b) shows the pose of compound 9. Whereas, compounds 10 and 19 poses are presented in panel (b) and (c), respectively.

In case of the ligands with alkoxy substituted aryl part only compounds **5** and **9** bearing single substitution at C-4' positions were found to be active. Both these compounds were found to be competitive inhibitors of *α*-glucosidase. A cursory look at the Figure-9(b) shows that the compound **9** anchors the active site *via* hydrophobic interactions with the residues in active site; Phe157, Pro240, His279 and Glu304. The π-stacking interaction between the benzothiazole ring of the compound and the residues of Phe157 might be the reason of the observed inhibition. Since, the residues of the hydrophobic patch partake in the catalysis by holding the terminal ring of acarbose [34].

Compound **10** bearing hydroxy and methoxy substitution on the aryl part is the most active member among the relevant derivatives **10**-**13**. The top ranked docked pose of the compound **10** showed similarity with the docked pose of compound **9** (Figure S3). The compound mediate hydrophobic interaction with Pro240 and Arg312 in the active site. The protein-inhibitor contact is further stabilized by π-stacking interaction between the compound and residues; Phe157 and His239 (Figure-9 (c)).

The binding mode of indole substituted aryl derivative **19** suggests that the compound is accommodated near the hydrophobic patch of the active site (Figure-9 (d)). The compound interact *via* hydrophobic interactions with the amino acids in the native contacts including; Phe157, Leu176, Pro240, Arg312, and His239. A halogen bond between Arg312 and the chloride moiety at the benzothiazole ring further stabilizes the contacts.

3. Conclusion

In this study *in vitro α*-gluocosidase inhibitory activity of twenty-four derivatives of 5-chloro-2-aryl benzo[d]thiazole was evaluated. Amongst them derivatives **1**-**5**, **9**-**11**, and **19** showed potent *α*-gluocosidase inhibitory activity than the drug acarbose used as a standard. The kinetics data indicated compounds **2**-**3**, **10**, **19**, and **25** as non-competitive, while **1**, **5**, **9**, and **11** as competitive inhibitors of *α*-gluocosidase. Moreover, *in silico* studies of active compounds with enzyme binding sites also employed to validate its the successful interactions with ligand proteins. These preliminary results identified compounds **1**-**5**, **9**-**11**, and **19** as lead molecules for further studies.

4. Experimental

4.1 Material and Methods

2-amino-4-cholorobenzenethiol, different aromatic aldehydes and solvents were purchased from Sigma-Aldrich USA and of analytical grade and were as used as without any further purification. Pre-coated silica gel, GF-254 (Merck, Germany) was used for thin layer chromatography. Visualization of TLC was performed under ultraviolet light at 254 and 366 nm. Mass spectra were carried out on a Finnigan MAT-311A (Germany) mass spectrometer. The ^{1}H-NMR were carried out on Avance Bruker AM spectrometers, operating at 300, and 400 MHz. The chemical shift values are presented in ppm (δ), relative to tetramethylsilane (TMS) as an internal standard and the coupling constant (J) are in Hz.

4.2. Bioassay for *α*-glucosidase inhibitory activity

α-Glucosidase inhibitory activity was evaluated by 0.1 M phosphate buffer (pH 6.8) at 37 °C. The enzyme (*S. cerevisiae* EC 3.2.1.20) was dissolved in phosphate buffer saline and incubated with different concentrations of test compounds at 37 °C for 15 min. *p*-Nitrophenyl-*α*-D-glucopyranoside (0.7 mM) was added, and change in absorbance at 400 nm was recorded for 30 min by multiplate reader. Test compounds were replaced with DMSO (7% final) in control. Acarbose was used as the standard inhibitor [35].

4.3. Statistical analyses

The IC_{50} values were estimated by using EZ-Fit Enzyme Kinetic Program (Perrella Scientific Inc., Amherst, USA) and the percent inhibition was calculated by using the subsequent formula

% Inhibition = 100 (100-OD test well/ OD control) X 100

4.3. Kinetic studies

The kinetic parameters of the *α*-glucosidase were analyzed by incubating the enzyme with different concentrations of test compounds. The concentrations of substrate were also varied (0.1- 0.8 mM) in order to evaluate the change in *K*m values.

4.4. Molecular docking Interaction

In order to predict the binding mode of newly synthesized benzothiazole derivatives, molecular docking studies were carried out with *α*-glucoronidase of *S. cerevisae* (yeast) using Glide software [29]. In order to compensate the non-availability of crystal structure, homology modeling was carried out using SWISS-MODEL web-server [36]. The FASTA sequence of *α*-glucosidase (P53051.1) of *S. cerevisiae* was obtained from NCBI protein database. The most reliable model was made using isomaltase (MAL12) from *S. cerevisiae* (PDB 3AJ7) exhibiting more than 85% similarity and 71% identity [32]. The developed model was submitted to server RAMPAGE for geometric analysis using the Ramachandran plot [31].

The builder module in MOE 2016.08 was used to draw the compounds. All the compounds were energy minimized, following the addition of partial charges as per Merck Molecular Force Field (MMFF94). The compounds were docked using Glide software. A receptor grid was generated suing the coordinates of the residues spanning the active site (Table-S1). All the compounds were docked using the default docking protocol in Glide and after post-docking minimization 10 poses of each

ligand were recoded for analysis. The resulting poses of the compounds were visually inspected to comprehend protein ligand interactions. The interactions were analyzed with the help of PLIP web server (https://projects.biotec.tu-dresden.de/plip-web/plip). All the visuals were recorded using Chimera [37].

4.5. General procedure for the syntheses of compounds 1-25

Synthesis of 2-amino-4-cholorobenzenethioles was carried out by reaction of 2-amino-4-cholorobenzenethiol with different aromatic aldehydes. In a representative reaction different aromatic aldehydes (1 mmol) and 2-amino-4-cholorobenzenethiol (1 mmol) were stirred in *N*,*N*-dimethylformamide (10 mL) as solvent for 30 minutes, then sodium metabisulfite ($Na_2S_2O_5$) 0.61 g was added into the mixture, and refluxed for 2 h. Progress of reaction was monitored by TLC. After completion of reaction, it was cooled and precipitated by addition of cool water. Filtration of precipitate, followed by washing with cool water, resulted in pure benzothiazoles **1-25**.

2-(5-Chlorobenzo[d]thiazol-2-yl)phenol (1)

White crystal, Yield: 83 %, M.P.: 198 °C, ^{1}H-NMR (300 MHz, CD_3OD) δ: 7.97 (d, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 7.83 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.41 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 7.38 (m, 2H, H-4', H-5'), 7.10 (d, 1H, $J_{6',5'}$ = 8.4 Hz, H-6'), 6.94 (d, 1H, $J_{3',4'}$ = 6.0 Hz, H-3'); EI-MS: *m/z* (rel. abund. %), 263 (M^+ +2, 37), 261 (M^+, 100), 233 (48), 206 (8), 198 (13), 142 (7), 107 (20). HREI-MS *m/z* : 261.0016, $[M]^+$ (Calcd for $C_{13}H_8ClNOS$, 261.0015).

4-(5-Chlorobenzothiazol-2-yl)phenol (2)

White solid, Yield: 70%, M.P.: 265 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.87 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.26 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 7.94 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.69 (d, 2H, $J_{2',3'}$, $J_{2',6'}$ = 8.7 Hz, H-2', H-6'), 6.85 (d, 2H, $J_{3',2'}$, $J_{5',6'}$ = 8.7 Hz, H-3', H-5'). EI-MS: *m/z* (rel. abund. %), 263(M^+ +2, 37), 261 (M^+, 94), 233(8), 142 (17), 107 (15). HREI-MS *m/z* : 261.0015 $[M]^+$ (Calcd for $C_{13}H_8ClNOS$, 261.0015).

3-(5-Chloro-2-benzothiazolyl)phenol (3)

White solid, Yield: 70%, M.P.: 196 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.80 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.32 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 2.1 Hz, H-6), 8.09 (d, 1H, $J_{4,6}$ = 2.1 Hz, H-4), 7.68 (s, 1H, H-2'), 7.03 (d, 1H, $J_{4',5'}$ = 7.8 Hz, H-4′), 7.37 (dd, 1H, $J_{5',4'}$ = 7.8 Hz, $J_{5',6'}$ = 7.5 Hz, H-5′), 7.56 (d, 1H,

$J_{6',5'}$ = 7.5 Hz, H-6′). EI-MS: *m/z* (rel. abund. %), 263 (M^+ +2, 37.8), 261 (M^+, 100), 232 (13), 142 (20), 130 (13), 107 (15). HREI-MS *m/z*: 261.0016 $[M]^+$ (Calcd for $C_{13}H_8ClNOS$, 261.0015).

4-Bromo-2-(5-chlorobenzothiazol-2-yl)phenol (4)

White crystal, Yield: 63%, M.P.: 210 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.81 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.39 (dd, 1H, $J_{6,7}$ = 8.7, $J_{6,4}$ =1.8 Hz, H-6), 7.97 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 6.97 (d, 1H, $J_{3',4'}$ = 9.0 Hz, H-3'), 7.44 (dd, 1H, $J_{4',3'}$= 9.0, $J_{4',6'}$ = 2.2 Hz, H-4'), 7.74 (d, 1H, $J_{6',4'}$ = 2.2 Hz, H-6'). EI-MS: *m/z* (rel. abund. %), 343 (M^++4, 28), 341 (M^+ +2, 100), 339 (M^+ 74.1), 261 (12), 232 (80), 197(30). HREI-MS *m/z* : 338.9120 $[M]^+$ (Calcd for $C_{13}H_7BrClNOS$, 338.9120).

5-Chloro-2-(4-methoxyphenyl)-benzothiazole (5)

White crystal, Yield: 82%, M.P.: 148 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.77 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.31 (dd, 1H, $J_{6,7}$ = 8.6 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 8.02 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.00 (d, 2H, $J_{2',3'}$, $J_{6',5'}$ = 8.7 Hz, H-2',H-6'), 7.99 (d, 2H, $J_{3',2'}$, $J_{5',6'}$ = 8.7 Hz, H-3', H-5′), 3.87 (s, 3H, OCH_3) . EI-MS: *m/z* (rel. abund. %), 277 (M^++2, 38), 275 (M^+, 100), 262 (19), 260 (49), 234 (19), 232 (52), 197 (25). HREI-MS *m/z* : 275.0174 $[M]^+$ (Calcd for $C_{14}H_{10}ClNOS$, 275.0172).

5-Chloro-2-(3,4-dimethoxyphenyl)-benzothiazole (6)

White solid, Yield: 80%, M.P.: 164 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.75 (d, 1H, $J_{7,6}$ = 8.5 Hz, H-7), 7.57 (dd, 1H, $J_{6,7}$ = 8.5, $J_{6,4}$ = 2.0 Hz, H-6), 8.07 (d, 1H, $J_{4,6}$= 2.0 Hz, H-4), 7.67 (d, 1H, $J_{2',6'}$ = 2.0 Hz, H-2'), 6.90 (d, 1H, $J_{5',6'}$ = 8.5 Hz, H-5′), 7.32 (dd, 1H, $J_{6',5'}$ = 8.5, $J_{6',2'}$ = 2.0 Hz, H-6′) . EI-MS: *m/z* (rel. abund. %), 307 (M^++2, 38), 305 (M^+, 100), 290 (3), 262 (29), 219 (14), 152 (9). HREI-MS *m/z*: 305.0277 $[M]^+$ (Calcd for $C_{15}H_{12}ClNO_2S$ 305.0278).

5-Chloro-2-(3,4,5-trimethoxyphenyl)benzo[*d*]thiazole (7)

White crystal, Yield: 89 %, M.P.: 159 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.74 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.34 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 8.07 (d, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 7.24 (s, 2H, H-2', H-6'). EI-MS: *m/z* (rel. abund. %), 337(M^+ +2, 39), 335 (M^+, 100), 322 (38), 320 (96), 294 (15), 277 (25), 262 (56), 249 (10). HREI-MS *m/z* : 335.0383 $[M]^+$ (Calcd for $C_{16}H_{14}ClNO_3S$, 335.0383).

5-Chloro-2-(2,3,4-trimethoxyphenyl)-benzothiazole (8)

White crystal, Yield: 75%, M.P.: 125 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 8.25 (d, 1H, $J_{6',5'}$ = 9.0 Hz, H-6'), 8.04 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.86 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.32 (dd, 1H, $J_{6,7}$ = 8.7, $J_{6,4}$ = 1.8 Hz, H-6), 6.83 (d, 1H, $J_{5',6'}$ = 9.0 Hz, H-5'); EI-MS: *m/z* (rel. abund. %), 337 (M^++2, 34), 335 (M^+, 80), 319 (100), 306 (28), 289 (28), 277 (38), 262 (22). HREI-MS *m/z* : 335.0385 $[M]^+$ (Calcd for $C_{16}H_{14}ClNO_3S$, 335.0383).

5-Chloro-2-(4-ethoxyphenyl)-benzothiazole (9)

Yellow solid, Yield: 41%, M.P.: 128 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.75 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.32 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 8.05 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 8.01 (d, 2H, $J_{2',3'}$, $J_{6',5'}$ = 8.7 Hz, H-2', H-6'), 6.98 (d, 2H, $J_{3',2'}$, $J_{5',6'}$ = 8.7 Hz, H-3',H-5'), 4.11 (q, 2H, OCH_2), 1.44 (t, 3H, CH_3). EI-MS: *m/z* (rel. abund. %), 291(M^+ +2, 38), 289.0 (M^+, 60), 261 (100), 232 (17), 197 (15), 142 (19), 107 (19). HREI-MS *m/z* : 289.0328 $[M]^+$ (Calcd for $C_{15}H_{12}ClNOS$, 289.0328).

2-(5-Chlorobenzothiazol-2-yl)-4-methoxyphenol (10)

White crystal, Yield: 81%, M.P.: 130 °C, ^{1}H-NMR: (300 MHz, $CDCl_3$): δ 7.76 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.36 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ =1.8 Hz, H-6), 7.96 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 6.97 (d, 1H, $J_{3',4'}$ = 8.0 Hz, H-3'), 7.06 (dd, 1H, $J_{4',3'}$ = 8.0 Hz, $J_{4',6'}$ = 2.4 Hz, H-4'), 7.16 (d, 1H, $J_{6',4'}$ = 2.4 Hz, H-6'). EI-MS: *m/z* (rel. abund. %), 293(M^+ +2, 38), 291 (M^+, 53), 278 (37), 276 (100), 220 (18), 194(16), 159 (10). HREI-MS *m/z* : 291.0121 $[M]^+$ (Calcd for $C_{14}H_{10}ClNO_2S$, 291.0121).

4-(5-Chlorobenzo[d]thiazol-2-yl)-2-methoxyphenol (11)

White solid, Yield: 86%, M.P.: 138 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.79 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.33 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 8.01 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.51 (dd, 1H, $J_{6',5'}$ = 8.1 Hz, $J_{6',2'}$= 1.8 Hz, H-6'), 6.99 (d, 1H, $J_{5',6'}$ = 8.4 Hz, H-5'), 7.74 (d, 1H, $J_{2',6'}$ = 1.8 Hz, H-2'). EI-MS: *m/z* (rel. abund. %), 293 (M^++2, 38), 291 (M^+, 100), 290 (40), 276 (16), 248 (28), 233 (6), 220 (8). HREI-MS *m/z* : 291.0121 $[M]^+$ (Calcd for $C_{14}H_{10}ClNO_2S$, 291.0121).

5-(5-Chlorobenzothiazol-2-yl)-2-methoxyphenol (12)

White solid, Yield: 90 %, M.P.: 140 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 8.01 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.76 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.69 (d, 1H, $J_{2',6'}$ = 2.1 Hz, H-2'), 7.33 (dd, 1H, $J_{6,7}$ = 8.7, $J_{6,4}$

= 1.8 Hz, H-6), 7.68 (dd, 1H, $J_{6',5'}$= 8.1 Hz, $J_{6',2'}$ = 2.0 Hz, H-6'), 6.94 (d, 1H, $J_{5',6'}$ = 8.1 Hz, H-5'); EI-MS: *m/z* (rel. abund. %), 293(M^+ +2, 38), 291 (M^+, 10), 276 (8), 248 (8), 235 (13), 197 (5), 155 (6). HREI-MS *m/z* : 291.0121 $[M]^+$ (Calcd $C_{14}H_{10}ClNO_2S$, 291.0121).

2-(5-Chlorobenzothiazol-2-yl)-6-methoxyphenol (13)

White solid, Yield: 89%, M.P.: 194 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 8.01 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.78 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.38 (d, 1H, $J_{6',5'}$ = 8.4 Hz, H-6'), 7.34 (dd, 1H, $J_{6,7}$ = 8.7, $J_{6,4}$ =1.8 Hz, H-6), 6.98 (d, 1H, $J_{4',5'}$ = 7.8 Hz, H-4'), 6.90 (t, 1H, $J_{5',6,4'}$ = 7.9 Hz, H-5'), EI-MS: *m/z* (rel. abund. %), 293 (M^++2, 38), 291(M^+, 92), 290 (44), 273 (51), 220 (30), 194 (16), 170 (11). HREI-MS *m/z* : 291.0121 $[M]^+$ (Calcd for $C_{14}H_{10}ClNO_2S$, 291.0121).

5-Chloro-2-phenylbenzothiazole (14)

White crystal, Yield: 92 %, M.P.: 135 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.80 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.34 (dd, 1H, $J_{6,7}$ = 8.4, $J_{6,4}$ = 2.0 Hz, H-6), 8.01 (d, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 8.07 (d, 2H, $J_{2',3'}$, $J_{6',5'}$ = 8.6 Hz, H-2',6'), 7.49 (m, 3H, H-3',H-4', H-5'). EI-MS: *m/z* (rel. abund. %), 247 (M^++2, 37), 245 (M^+, 100), 218 (6), 210 (10), 142 (56), 122 (15), 107 (35). HREI-MS *m/z* : 245.0066 $[M]^+$ (Calcd for $C_{13}H_8ClNS$, 245.0066).

5-Chloro-2-(4-chlorophenyl)-benzothiazole (15)

White solid, Yield: 73%, M.P.: 158 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.79 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.35 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 8.02 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.98 (d, 2H, $J_{2',3'}$, $J_{6',5'}$ = 8.7, Hz, H-2',H-6'), 7.46 (d, 2H, $J_{3',2'}$, $J_{5',6'}$ = 8.7 Hz, H-3', H-5'). EI-MS: *m/z* (rel. abund. %), 281(M^+ +2, 69.5), 279 (M^+, 100), 244 (44), 273 (51), 142 (30), 137 (12), 107 (25). HREI-MS *m/z* : 278.9677 $[M]^+$ (Calcd for $C_{13}H_7Cl_2NS$, 278.9676).

5-Chloro-2-(2,4-dichlorophenyl)-benzothiazole (16)

White solid, Yield: 59%, M.P.: 203 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 8.05 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.55 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 2.1 Hz, H-6), 8.09 (d, 1H, $J_{4,6}$ = 2.1 Hz, H-4), 7.73 (d, 1H, $J_{3',5'}$ = 2.1 Hz, H-3'), 7.50 (dd, 1H, $J_{5',6'}$ = 8.4 Hz, $J_{5',3'}$ = 1.8 Hz, H-5′), 8.25 (d, 1H, $J_{6',5'}$ = 8.4 Hz, H-6′). EI-MS: *m/z* (rel. abund. %), 316 (M^+ +2, 35.6), 314 (M^+, 100), 312 (92), 277 (5.0), 142 (20), 107 (11). HR-EIMS *m/z*: 314.9257 $[M]^+$ (Calcd for $C_{13}H_6Cl_3NS$, 314.9257).

4-(5-Chlorobenzothiazol-2-yl)-*N*,*N*-dimethylaniline (17)

White solid, Yield: 68%, M.P.: 172 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.71 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.26 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 7.99 (d, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 7.94 (d, 2H, $J_{2',3'}$, $J_{6',5'}$ = 8.6 Hz, H-2',6'), 6.76 (d, 2H, $J_{3',2'}$, $J_{5',6'}$ = 8.6 Hz, H-3', H-5′), 3.06 (s, 6H,$(CH_3)_2$). EI-MS: *m/z* (rel. abund. %), 290 (M^++2, 36), 288 (M^+, 100), 287 (99), 274 (15), 272 (20), 259 (25), 244 (11), 143 (23). HREI-MS *m/z* : 288.0489 $[M]^+$ (Calcd for $C_{15}H_{13}ClN_2S$, 288.0488).

5-Chloro-2-(naphthalen-2-yl)-benzothiazole (18)

White crystal ,Yield: 59 %, M.P.: 152 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.83 (d, 1H, $J_{7,6}$ = 8.5 Hz H-7), 7.37 (dd, 1H, $J_{6,7}$ = 8.5 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 8.07 (d, 1H, $J_{4,6}$ = 2.0 Hz, H-4), 7.90 (d, 1H, $J_{1',3'}$ = 1.5 Hz, H-1'), 8.17 (dd, 1H, $J_{3',4'}$ 8.5 Hz, $J_{3',1'}$ = 1.5 Hz, H-3′), 7.95 (d, 1H, $J_{4',3'}$ = 8.5 Hz, H-4′), 7.98 (d, 1H, $J_{5',6'}$ = 8.0 Hz, H-5′), 7.87 (t, 1H, H-6′), 7.56 (m, 2H, H-7′, H-8'). EI-MS: *m/z* (rel. abund. %), 297 (M^+ +2, 38), 295 (M^+, 100), 235 (18), 233 (49), 207 (9), 198 (13), 107(16). HREI-MS *m/z* : 295.0224 $[M]^+$ (Calcd for $C_{17}H_{10}ClNS$, 295.0222).

5-Chloro-2-(1H-indol-3-yl)-benzothiazole (19)

Brown solid, Yield: 69%, M.P.: 200 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.74 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.34 (m, 2H, H-6, 5'), 8.28 (brs, 2H, H-4, H-7'), 8.06 (s, 1H, H-2′), 7.52 (d, 1H, $J_{4',5}$ = 8.2 Hz, H-4′), 8.09 (t, 1H, $J_{6',5',7'}$ = 8.3 Hz, H-6′). EI-MS: *m/z* (rel. abund. %), 286 (M^++ 2, 38), 284(M^+, 99), 259 (257), 22 (5), 158 (100), 124 (30). HREI-MS *m/z* : 284.0176 $[M]^+$ (Calcd for $C_{15}H_9ClN_2S$, 284.0175).

5-Chloro-2-(furan-2-yl)-benzothiazole (20)

White crystal, Yield: 82%, M.P.: 121 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.79 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.35 (dd, 1H, $J_{6,7}$ = 8.4, Hz $J_{6,4}$ = 1.8 Hz, H-6), 8.01 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.21 (d, 1H, $J_{2',3'}$ = 0.9 Hz, H-2'), 6.59 (q, 1H, H-3'), 7.60 (d, 1H, $J_{4',3'}$ = 3.0 Hz, H-2'). EI-MS: *m/z* (rel. abund. %), 237(M^+ +2, 37), 235 (M^+, 100), 244 (44), 273 (51), 142 (30), 137 (12), 107 (25). HREI-MS *m/z* : 234.9859 $[M]^+$ (Calcd for $C_{11}H_6ClNOS$, 234.9859).

5-Chloro-2-(5-methylfuran-2-yl)benzothiazole (21)

White solid, Yield: 46%, M.P.: 164 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.74 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.30 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 7.97 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.09 (d, 1H, $J_{3',4'}$ = 3.0 Hz, H-3'), 6.19 (d, 1H, $J_{4',3'}$ = 2.4 Hz, H-4'), 2.42 (s, 3H, CH_3). EI-MS: *m/z* (rel. abund. %), 251(M^+ +2, 37), 249 (M^+, 100), 248 (35), 234 (29), 220 (60), 206 (28), 179 (5). HREI-MS *m/z* : 249.0015 $[M]^+$ (Calcd for $C_{12}H_8ClNOS$, 249.0015).

5-Chloro-2-(thiophen-2-yl)-benzothiazole (22)

White solid, Yield: 86 %, M.P.: 120 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.74 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.33 (dd, 1H, $J_{6,7}$ = 8.4 Hz, $J_{6,4}$ = 1.8 Hz, H-6), 7.99 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 7.66 (d, 1H, $J_{2',3'}$ = 3.0 Hz, H-2'), 7.13 (t, 1H, H-3'), 7.52 (d, 1H, $J_{4',3'}$= 4.8 Hz, H-4'). EI-MS: *m/z* (rel. abund. %), 253 (M^++2, 41), 251 (M^+, 100), 218(5), 207 (8), 142 (27), 125 (7), 107 (18). HREI-MS *m/z* : 250.9631 $[M]^+$ (Calcd for $C_{11}H_6ClNS_2$, 250.9630).

5-Chloro-2-(pyridin-3-yl)-benzothiazole (23)

White solid, Yield: 93%, M.P.: 172 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.83 (d, 1H, $J_{7,6}$ = 8.4 Hz, H-7), 7.39 (dd, 1H, $J_{6,7}$ = 8.4, $J_{6,4}$ = 1.8 Hz, H-6), 8.05 (d, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 9.27 (d, 1H, $J_{2',6'}$ = 1.8 Hz, H-2'), 8.73 (d, 1H, $J_{4',5'}$ = 3.9 Hz, H-4'), 7.50 (dd, 1H, $J_{5',4'}$ = 5.0 Hz, $J_{5',6'}$ =7.8 Hz, H-5'), 8.42 (dd, 1H, $J_{6',2'}$, = 1.8 Hz, $J_{6',5'}$ =6.6 Hz, H-6'). EI-MS: *m/z* (rel. abund. %), 248 (M^++2, 37.5), 246 (M^+, 100), 220 (25), 211(5), 194 (4), 142 (12), 107 (20). HREI-MS *m/z* : 246.0019 $[M]^+$ (Calcd for $C_{12}H_7ClN_2S$, 246.0018).

5-Chloro-2-(pyridin-4-yl)-benzothiazole (24)

White crystalline solid, Yield: 87%, M.P.: 185 °C, ^{1}H-NMR: (300 MHz, CD_3OD): δ 7.83 (d, 1H, $J_{7,6}$ = 8.7 Hz, H-7), 7.41 (dd, 1H, $J_{6,7}$ = 8.7 Hz, $J_{6,4}$ = 2.0 Hz, H-6), 8.08 (d, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 8.76 (d, 2H, $J_{2',3'}$, $J_{2',6'}$ = 6.0 Hz, H-2', 6'), 7.93 (d, 2H, $J_{3',2'}$, $J_{6',2'}$ = 6.0 Hz, H-3', 6'). EI-MS: *m/z* (rel. abund. %), 248 (M^+ + 2, 37), 246 (M^+, 100), 235 (18), 233 (47), 207 (9), 198 (15), 117 (9). HREI-MS *m/z* : 246.0019, $[M]^+$ (Calcd for $C_{12}H_7ClN_2S$, 246.0018).

5-Chloro-2-(4-(pentyloxy)phenyl)benzothiazole (25)

White solid, Yield: 41%, ^{1}H-NMR: (400 MHz, DMSO): δ 8.21 (d, 1H, $J_{7,8}$ = 8.8 Hz, H-7), 8.19 (m, 2H, H-2', H-3'), 8.13 (s, 1H, H-5), 7.53 (dd, 1H, $J_{8,7}$ = 8.4 Hz, $J_{8,5}$ = 2.0 Hz, H-8), 7.36 (d, 2H, $J_{5',6'}$, $J_{6',5'}$ = 8.4 Hz, H-5',H-6'), 4.12 (q, 2H, 4"-CH_2), 3.16 (m, 2H, 2"-CH_2). 2.62 (m, 2H, 3"-CH_2), 2.62 (m, 2H, 1"-CH_2), 1.00 (t, 3H, 5"-CH_3), EI-MS: *m/z* (rel. abund. %), 333 (M^+ +2, 2.5), 331.0 (M^+, 8.9), 261 (100.0), 232 (4.6), 197 (3.1), 142 (3.5), 107 (2.4), HREI-MS *m/z* : 331.0798, $[M]^+$ (Calcd for $C_{18}H_{18}ClNOS$, 331.0799)

Conflict of Interest

Authors declare no conflict of interest.

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Synthesis, α-Glucosidase Inhibitory Potential in vitro and in silico studies of 5-Chloro-2-Aryl Benzo[d]thiazoles: An Approach to Control Diabetes Mellitus

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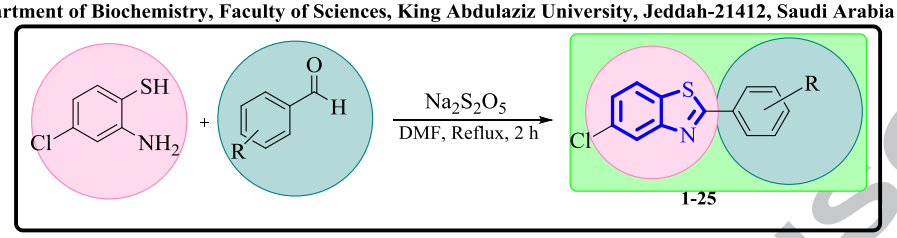

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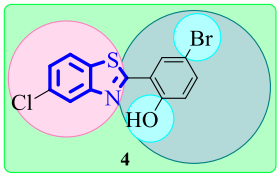

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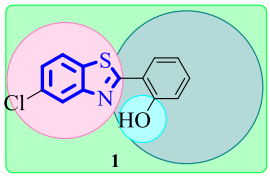

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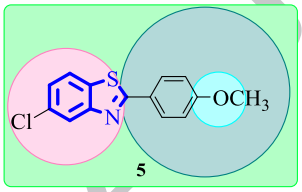
IC_{50} = 136.2 ± 5.7 μM



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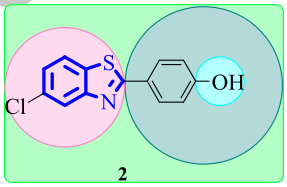
IC_{50} = 53.4 ± 4.3 μM



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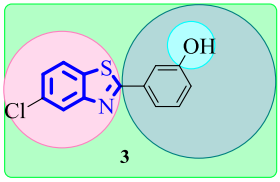

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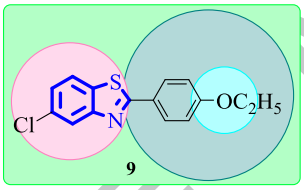

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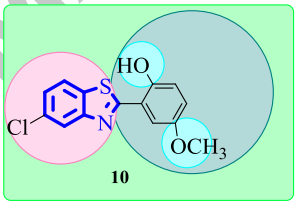
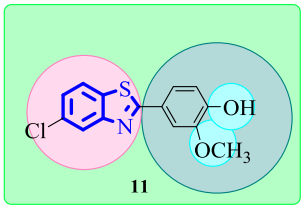
IC_{50} = 24.8 ± 0.4 μM



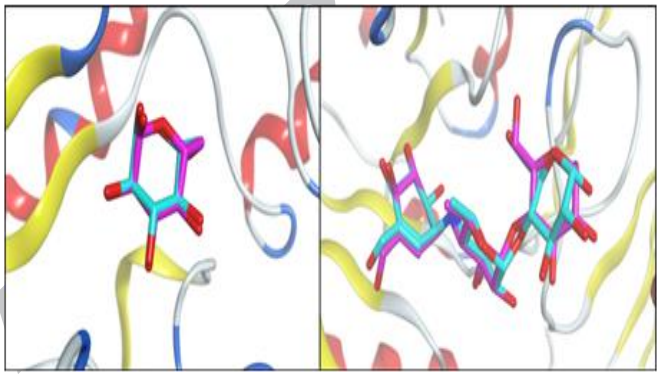
10

IC_{50} = 25.6 ± 1.5 μM

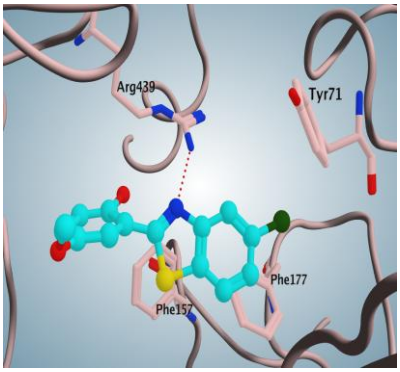


11

IC_{50} = 52.7 ± 1.07 μM



The redocking poses of α-D-glucose (left)and Acarbose (right). The crystal poses are presented as cyan sticks while the docked poses are depicted as magenta sticks



The graphics presenting the binding mode of the benzothiazole part of the ligands. Here the docked pose of compound (5) is presented as representative structure. The red dotted lines highlight the hydrogen bond

Research Highlight

- Synthesis of 5-chloro-2-aryl benzo[*d*]thiazoles has been performed
- *α*-Glucosidase Inhibitory potential of synthetic compounds has been evaluated.
- *In silico* studies of 5-chloro-2-aryl benzo[*d*]thiazoles have been accomplished
- All synthetic compounds were spectroscopically characterized.
- Structure-activity relationship has been evaluated.