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Graphical Abstract

Syntheses of New 3-Thiazolyl Coumarin Derivatives, *In Vitro* α-Glucosidase Inhibitory Activity, and Molecular Modeling Studies

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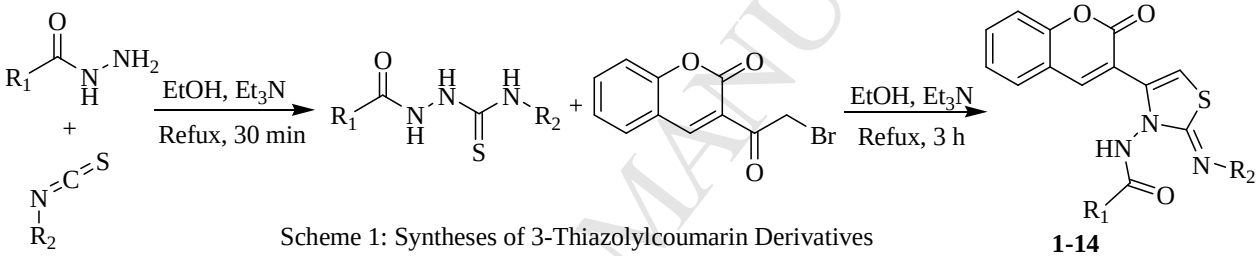
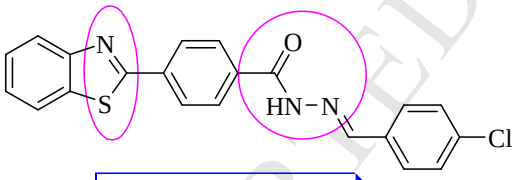
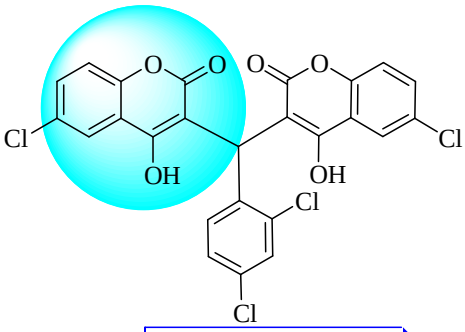


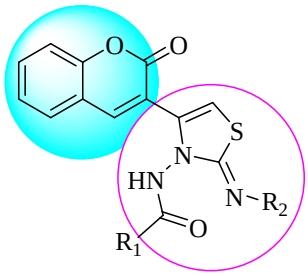
Scheme 1: Syntheses of 3-Thiazolylcoumarin Derivatives



IC_{50} = 5.31 ± 0.03 μM



IC_{50} = 16.54 ± 0.36 μM



Synthetic Derivatives 1-14 (IC_{50} = 0.12 ± 0.01-16.20 ± 0.23 μM)

Standard Acarbose (IC_{50} = 38.25 ± 0.12 μM)

Syntheses of New 3-Thiazolyl Coumarin Derivatives, *In Vitro* α-Glucosidase Inhibitory Activity, and Molecular Modeling Studies

Uzma Salar,[a] Muhammad Taha,*[b,c] Khalid Mohammed Khan,*[a] Nor Hadiani Ismail,[b,c] Syahrul Imran,[b,c] Shahnaz Perveen,[d] Sahib Gul,[e] Abdul Wadood[e]

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[b]*Atta-ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor D. E., Malaysia*
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[d]*PCSIR Laboratories Complex, Karachi, Shahrah-e-Dr. Salimuzzaman Siddiqui, Karachi-75280, Pakistan*
[e]*Department of Biochemistry, Computational Medicinal Chemistry Laboratory, UCSS, Abdul Wali Khan University, Mardan, Pakistan*

Abstract: 3-Thiazolylcoumarin derivatives **1-14** were synthesized *via* one-pot two step reactions, and screened for *in vitro* α-glucosidase inhibitory activity. All compounds showed inhibitory activity in the range of IC_{50} = 0.12 ± 0.01-16.20 ± 0.23 μM as compared to standard acarbose (IC_{50} = 38.25 ± 0.12 μM), and also found to be nontoxic. Molecular docking study was carried out in order to establish the structure-activity relationship (SAR) which demonstrated that electron rich centers at one and electron withdrawing centers at the other end of the molecules showed strong inhibitory activity. All the synthesized compounds were characterized by spectroscopic techniques such as EI-MS, HREI-MS, ^{1}H-NMR and ^{13}C-NMR. CHN analysis was also performed.

Keywords: Synthesis; 3-Thiazolylcoumarin; α-Glucosidase; Structure-activity relationship; Docking studies, Diabetic complications; Acarbose.

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Introduction

Being important class of heterocyclic compounds, coumarins have been reported to exhibit wide spectrum of biological activities, and continuously upraised significant attention of researchers due to valuable consequences on human health as well as lesser toxicity [1,2]. A wide spectrum of pharmacological activities was associated with coumarins such as antioxidant [3,4], antiinflammatory [5], anticoagulant [6], antibacterial [7], cytotoxic effects [8,9], anticancer [10], antiHIV [11,12] and dyslipidemic activities [13]. Coumarin derivatives also reported as vasorelaxant [14], free radical scavengers [15], triplet sensitizers [16] and lipid-lowering agents [17].

Heterocyclic ring thiazole has the privilege to be the core part of medicinally important compounds [18], due to its noteworthy pharmacological activities including anti-inflammatory [19], anticonvulsant [20], analgesic [21], pesticidal [22], antiviral [23], antituberculosis [24], antimicrobial agents, anticancer [25], antitumor [26] and enzyme inhibition activities [27]. Thiazole scaffold has also reported to possess medicinal applications in hypertension [28], schizophrenia [29], and in the cure of allergies [30].

α-Glucosidase enzyme catalyzes the breakdown of polysaccharides into monosaccharides which are able to absorb in small intestine and leads to diabetes mellitus. Type II diabetes is the most common type and responsible for nearby 5% death globally [31]. *α*-Glucosidase enzyme catalyzes the reaction by hydrolyzing the *α*-glucosidal bond of isomaltose oligosaccharides (linear and branched) and releases free *α*-D-glucose which is mainly responsible to cause hyperglycemia [32]. Inhibition of enzyme activity is one of the simplest way to treat type II diabetes mellitus by slowing the absorption process of glucose in intestine [33]. Amongst the *α*-glucosidase inhibitors, acarbose, miglitol, and voglibose are being clinically used for the cure of type II diabetes mellitus [34-36] and also used as antidiabetic, anticancer and antiHIV agents [37-39]. Unfortunately, these are 50% less effective than other antidiabetic agents such as sulfonylurea and metformin. These medications are also associated with some side effects which include diarrhea, flatulence and abdominal discomfort [40]. So, it is limiting factor to use the drug alone and often use in combination with other antidiabetic drugs to improve the efficacy.

Our research group has identified a number of heterocyclic compounds for their effectiveness in medicinal chemistry [41-47] and has already published coumarin and thiazole as potential classes

of α-glucosidase inhibitors, separately, (Figure-1) [48,49] which prompted us to broaden the spectrum of our research for further evaluation of these heterocycles in search of potent α-glucosidase inhibitor. Therefore, we designed a hybrid scaffold by incorporating all pharmacophores (coumarin, thiazole, hydrazide) in a single molecule to check the α-glucosidase inhibition. New skeleton of 3-thiazolylcoumarin derivatives **1-14** were synthesized *via* "one pot" two step reaction. The reaction is well suited as high atom economic in industrial process due to bringing out three pharmaceutically active pharmacophores within a single scaffold with lack of hazardous wastes. To the best of our knowledge, the synthesized compounds are never reported before chemically and medicinally. Superior activities of compounds **1-14** against α-glucosidase enzyme in comparison of standard acarbose proved our hypothesis. All compounds found to be non-cytotoxic.

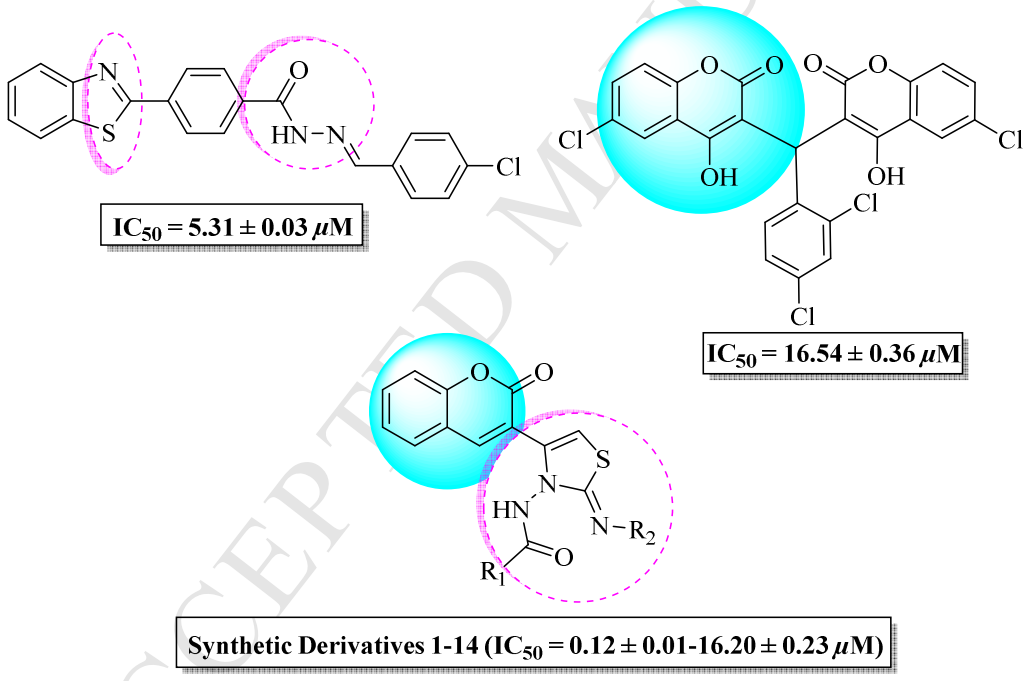


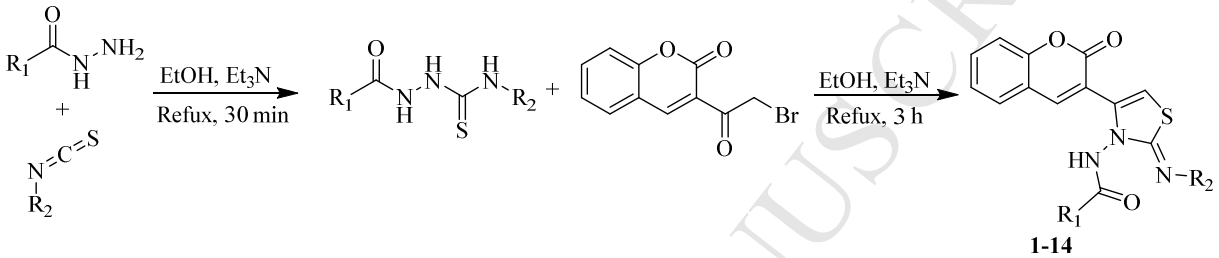
Figure-1: Rationale of the Current Study

Results and Discussion

Chemistry

3-Thiazolylcoumarin derivatives were synthesized by "one pot" two step reaction. In first step, different benzohydrazide derivatives were treated with commercially available benzene isothiocyanates in ethanol (Scheme-1), to afford thiosemicarbazide intermediates within 30

minutes. In second step, resulted intermediate undergo cyclization reaction when treated with 3-(bromoacetyl) coumarin in presence of catalytic amount of trimethylamine, to afford 3-thiazolylcoumarin derivatives. Reaction mixture was refluxed for 3 h to afford the products in the form of precipitates which were collected *via* filtration and crystallized from ethyl acetate to get the pure products in high yields. Synthesized derivatives **1-14** were characterized by different spectroscopic techniques EI-MS, HREI-MS, ^{1}H-NMR and ^{13}C-NMR. CHN analysis was also performed.



Scheme 1: Syntheses of 3-Thiazolylcoumarin Derivatives

Stereochemical Assignment of Iminic Double Bond by NOESY

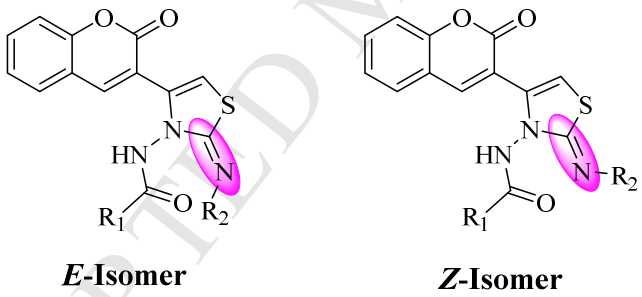
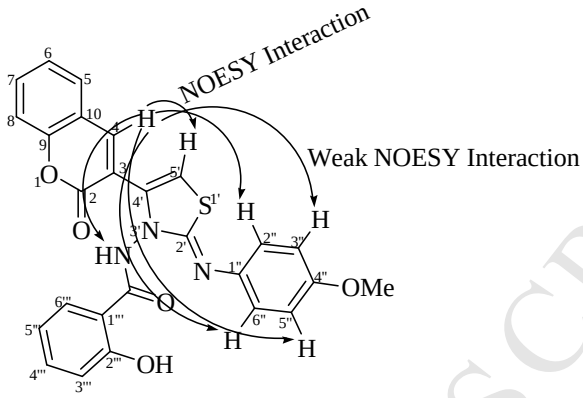


Figure-2: Isomers of Products

Purity of ^{1}H-NMR spectra of all compounds showed the formation of single isomer, either (*Z*) or (*E*) (Figure-2). However, in order to confirm the stereochemistry of iminic double bond, nuclear overhauser enhance spectroscopy (NOESY) was performed on one of the synthesized compounds. Spectrum showed many NOESY interactions, some of them confirmed the (*Z*) stereochemistry of the compounds. Amidic NH and H-5′ of thiazole moiety showed strong NOESY interaction with H-4 of coumarin ring, as these parts of the molecule are close in space. The distinctive weak NOESY interaction of H-2″, 6″ and H-3″, 5″ with the H-4 of coumarin as well as the absence of NOESY interaction with the 2-hydroxy benzamide ring confirmed that the

ring is close in space with coumarin ring as well as far apart from the benzamide ring. These observations confirmed the *Z* stereochemistry of the iminic double bond (Figure-3a).

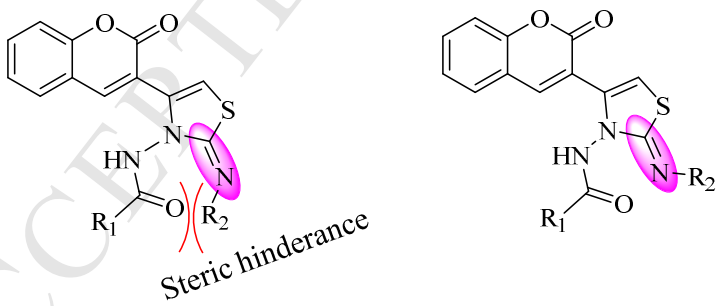


Compound 9

Bold double headed arrow = Strong NOESY interaction
Dashed double headed arrow = Weak NOESY interaction

Figure-3a: NOESY Interactions between Protons of Compound 9

Figure-3b clearly displayed that the formation of *Z*-isomer is more favorable as compare to *E*-isomer. As in case of *Z*-isomer, rings R_1 and R_2 are far apart from each other and free from steric any hindrance, however, R_1 and R_2 are much closed in *E*-isomer to create steric hindrance, and brings out the instability in the molecule.

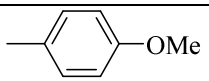
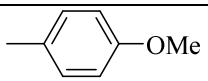
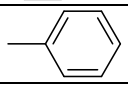
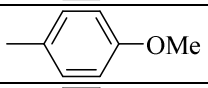
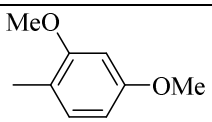
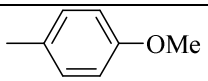
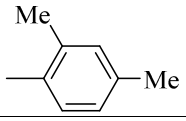
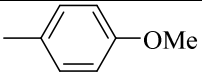
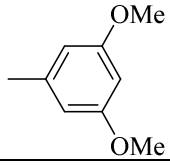
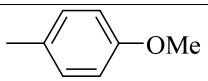
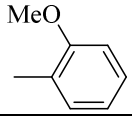
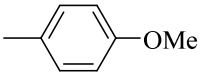
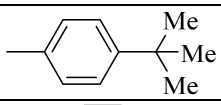
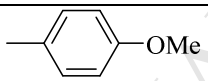
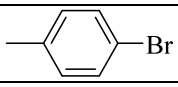
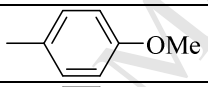
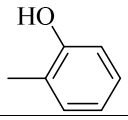
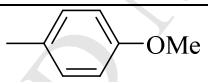
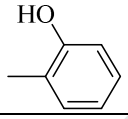
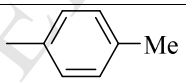
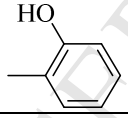
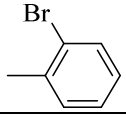
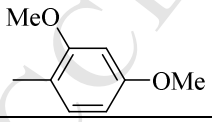
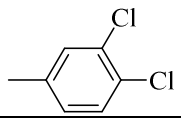
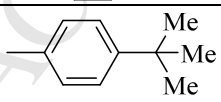
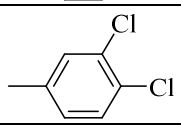
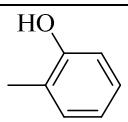
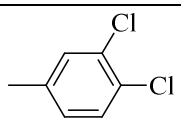


Unstable *E*-Isomer **More Stable *Z*-Isomer**

Figure-3b: Comparison of Stability of *E*- and *Z*-Isomer

Table-1: *In vitro* α-glucosidase inhibitory activity and docking scores of 3-thiazolylcoumarin derivatives **1-14**

Comp. No.	R_1	R_2	(IC_{50} ± SEM)[a]	Docking (S) Score

1			3.60 ± 0.04	-14.1421
2			6.50 ± 0.06	-12.2064
3			7.40 ± 0.07	-14.5631
4			2.90 ± 0.03	-14.4937
5			8.10 ± 0.07	-12.8795
6			16.20 ± 0.23	-13.9285
7			1.40 ± 0.02	-15.6593
8			9.45 ± 0.12	-13.7128
9			1.10 ± 0.01	-15.8567
10			9.19 ± 0.14	-13.9671
11			4.06 ± 0.05	-13.3335
12			2.50 ± 0.03	-14.5165
13			0.78 ± 0.01	-16-1050
14			0.12 ± 0.01	-16.5279
[b]Standard = Acarbose		38.25 ± 0.12		

[a]IC_{50} values are expressed as mean ± standard error of mean; [b]Standard inhibitor for α-glucosidase.

α-Glucosidase Inhibitory Activities

All the synthetic compounds were screened to check their *in vitro* *α*-glucosidase inhibitory activity. Results showed that all compounds found to have excellent inhibitory activity in the range of IC_{50} = 0.12 ± 0.01-16.20 ± 0.23 μM, when compared to the standard acarbose (IC_{50} = 38.25 ± 0.12 μM) (Table-1). 2*H*-Chromen-2-one moiety, thiazole as well as arene rings were collectively played vital role in exhibiting the activity. However, it was observed that compounds having both electron donating and withdrawing groups displayed strong potential. To verify these observations molecular docking study was performed. Cytotoxic studies demonstrated that these compounds are also non-cytotoxic.

Molecular Docking

There was two aims of docking studies: specific structural modeling and accurate prediction of activity [50]. Molecular docking protocol applied to find out the interactions between inhibitors and active site of the target protein. To study the interactions of molecular recognition, MOE-Dock method was utilized [51] which allows the ligands to be flexible during docking so that the ligands can adjust their different conformations in the binding pocket of the receptor. 3D structures of the 3-thiazolylcoumarin derivatives were built in builder tool of MOE and 3D protonation. Energy minimization was carried out for each compound and saved in mdb file for further assessment in molecular docking. 3D Modeled structure of the *α*-glucosidase was 3D protonated and then energy minimization was carried out and allowed the protein to dock to the fourteen synthetic compounds with most of the default parameters of the MOE. However, for the best results, we also applied refinement “forcefield” and rescoring function “London dG” implemented in MOE docking protocol. The binding mode of the ligands in the pocket of the protein was predicted by using the Pymol software.

Interactions Detail

All the synthetic compounds showed significant *in-silico* inhibitory activities. The compounds ranging from **1**-**9** have same R_2 substituent *i.e.*, methoxy benzene but different R_1 groups (Table-1). Among these compounds, the better interaction modes were observed for compounds **4** and **7**. Compound **7** showed the docking score of **-15.6593** and its docking analysis revealed that this compound formed three interactions with the residues Phe157, Tyr313 and Arg312 of the target

protein. Phe300 involved in arene-cation interaction with the benzene ring of the 2*H*-chromen-2-one moiety and Arg312 formed another arene-cation interaction with *tert*-butyl benzene group of the compound. However, Tyr313 interact with the lone pair of oxygen of methoxy benzene as given in the Figure-4b. Compound **4** showed the docking score **-14.4937** and the 3D interaction binding mode of the compound was observed having three interactions with the residues His279, Arg312 and Asn347. Arene-cation interaction was observed between His279 and π electrons of the dimethyl benzene moiety of the compound. Arg312 displayed arene-cation interaction with the 2*H*-chromen-2-one moiety of the same ligand. Asn347 formed polar interaction with the oxygen of 2*H*-chromen-2-one group of the inhibitor as shown in the Figure-4a. The increased activities and good predicted interactions of these compounds might be due to the presence of the species having electron donating inductive effect (R_1) *i.e. tert*-butyl (compound **7**) and dimethyl (compound **4**) as compare to compounds **2**, **3**, **4**, **5**, **6** and **8** (Table-1). Comparatively, more active compound **9** (from **1**-**9**) displayed three polar interactions with the residues Asn241 and Arg312 with the docking score **-15.8567**. Asn241 interacted with the lone pair of the keto-oxygen of 2*H*-chromen-2-one moiety, whereas Arg312 established two interaction with oxygen atom of methoxy benzene group of the ligand (Figure-5b). The phenolic group at R_1 position is not directly involved in bonding with the receptors atoms, however, it increased the overall polarizability of the compound. The good biological activity observed for compound **9** as compare with compound **4** and **7** might be due to the establishment of three polar interactions with the active site residues, whereas only single polar contact was observed in case of compounds **4** and **7** (Figure-4a and 4b). Compound **1** having methoxy group at *para* position (R_1) showed two interactions with the residues Tyr313 and Phe300 of the receptor protein (Figure-5a), while compound **6** with methoxy group at *ortho* position (R_1) displayed only one arene-cation interaction with the residue His279. Similarly, compound **3**, having two methoxy groups (R_1) at *ortho* and *para* positions, and compound **5**, with two methoxy groups at two *meta* positions, both displayed two interactions with Phe300, Asn347 and Tyr313, Asn347, respectively. The positions of the methoxy groups in these two compounds showed negligible effect in the *in-silico* study. The docking scores for all compounds are given in Table-1. Compound **8** with bromo benzene substituent at R_1 also showed two interactions. Arg312 formed arene-cation contact with bromo benzene moiety and His279 established the same contact with the 2*H*-chromen-2-one moiety of the compound.

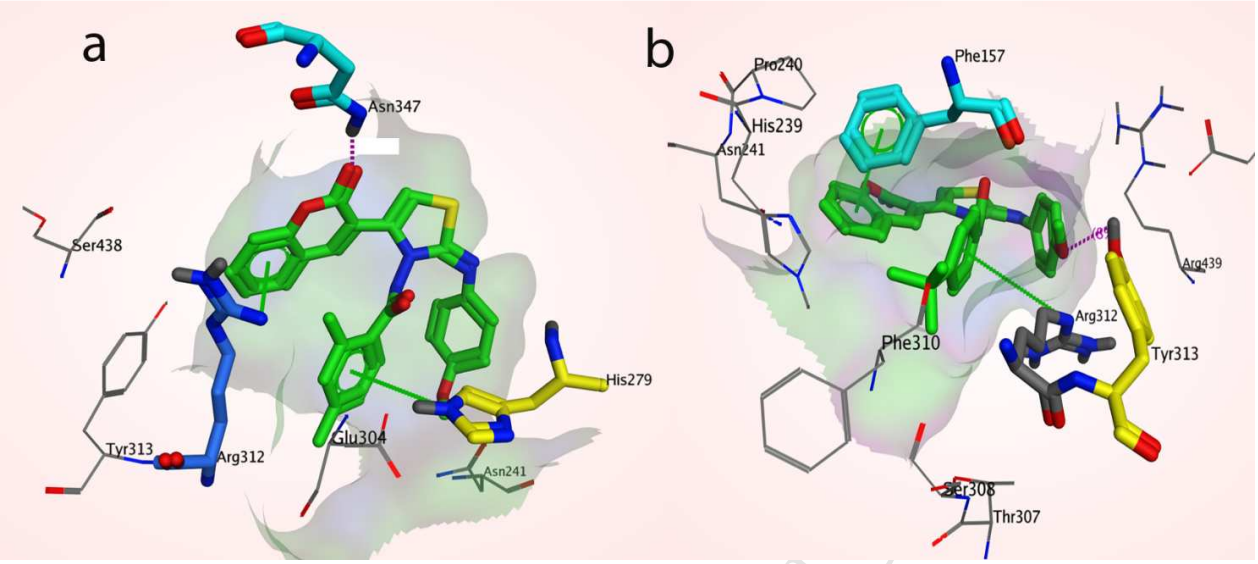


Figure-4: Docked conformer of the compounds **4 (a)**, **7 (b)** and their interactions with the residues of the α-glucosidase protein.

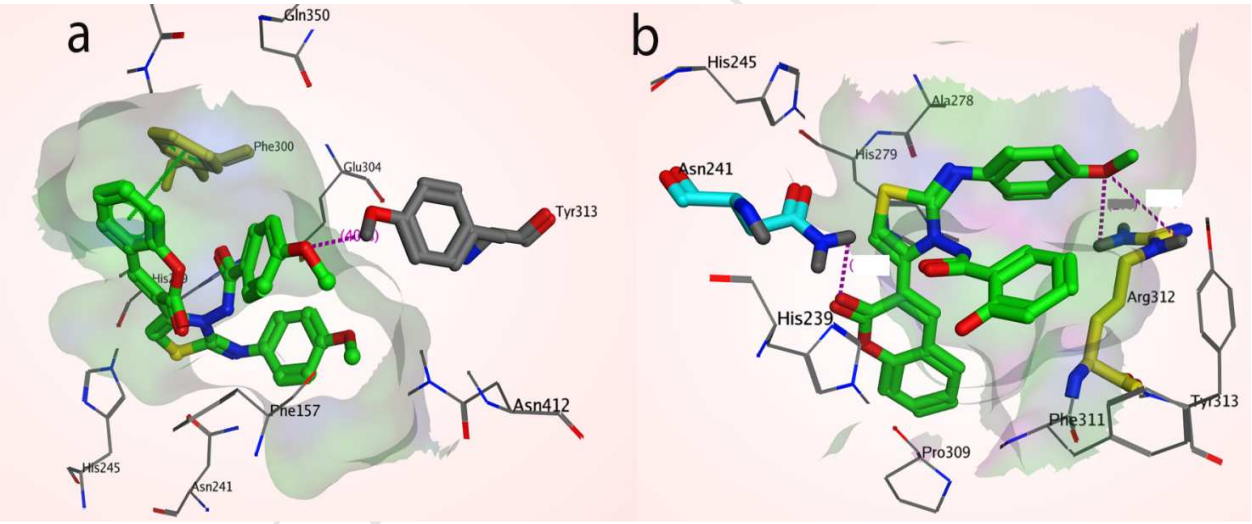


Figure-5: Docked conformer of the compound **1(a)**, **9 (b)** and their interactions with the residues of the α-glucosidase protein.

Among the compounds (**10**-**14**), compounds **12**, **13** and **14** having similar group (dichloro benzene) at R_2 but different groups at R_1 position (Table-1) showed three interactions with the active site residues. Compound **12** with two methoxy groups at *ortho* and *para* positions (R_1) interacted with the residues Phe300, Tyr313 and Asn241. Phe300 formed arene-arene contacts with the 2*H*-chromen-2-one moiety and Tyr313 interacted with the oxygen of methoxy group of the compound. Asn241 bonded to the N atom of amidic moiety as presented in Figure-6a. Due to the presence of the electron donating groups (OMe) on one side and electron withdrawing groups

(Cl) on the other side of the compound might be the reason of its polarizability and hence good activity.

Compound **13** with *tert*-butyl benzene at R_1 also formed three interactions with the active residues of the target protein as shown in the Figure-6b. Phe157 and Arg439 formed arene-arene contact with the π electrons of *tert*-butyl benzene moiety and a polar bond with the oxygen atom of the 2*H*-chromen-2-one group of the compound. Tyr313 bonded to the N atom of amidic moiety. The activity of compound **13** might be driven by the polarizability as in case of compound **12**, due to the presence of electron donating group (*tert*-butyl) at one end and electron withdrawing groups (Cl) at another end. Comparing the structures of compounds **13** and **7** which have about similar structures, the only difference is at R_2 position (Table-1). As a result of structural similarity, both compounds showed interaction with almost similar active site residues *i.e.* Phe157 and Tyr313 (Figure-4b and 6b). The minor difference in observed interactions for compounds **7** and **13** might be due to the difference in geometries of these molecules attributed by structural difference at R_2 position.

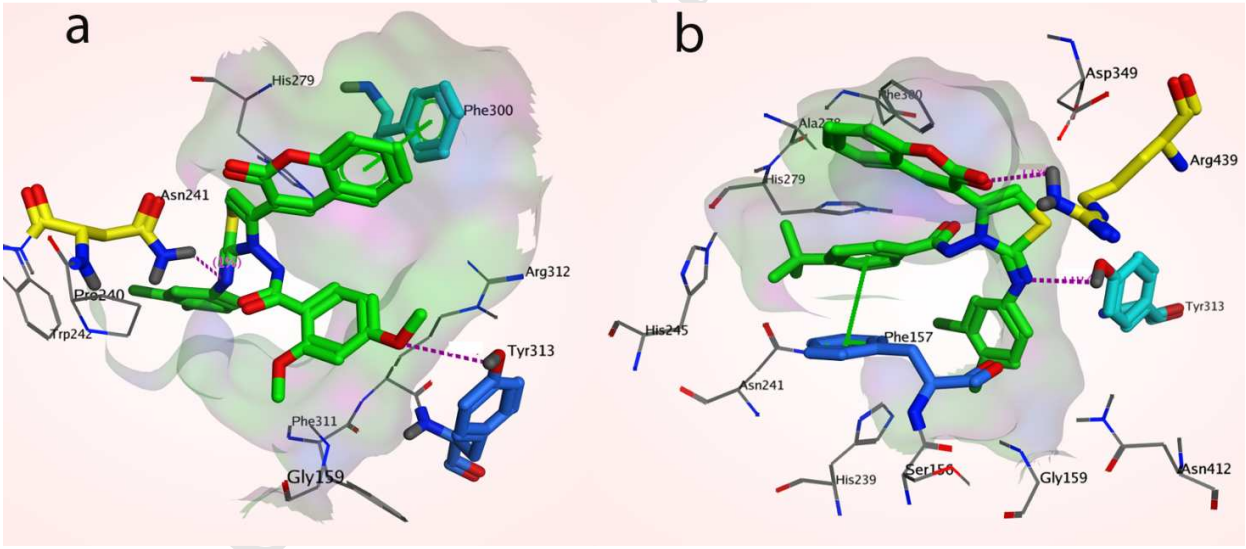


Figure-6: Docked conformer of the compound **12 (a)**, **13 (b)** and their interactions with the residues of the α-glucosidase protein.

The 3D binding mode of compound **14**, the most active compound in the series, showed three interactions with the residues Phe300, Arg312 and Asn241. Arene-arene interaction was observed between Phe300 and π electrons of the dichloro benzene group of the compound. Arg312 displayed arene-cation interaction with the phenolic part of the ligand. Asn241 formed

polar interaction with the oxygen of 2*H*-chromen-2-one group of the inhibitor as shown in the Figure-7. Unfortunately, we are unable to explain the good activity of compound **14** as compare to compounds **12** and **13**. This might be due to the minor difference in nature of substituents present at R_1 position in these compounds as these groups have about similar electron donating effect.

In case of compounds **9**, **10**, **11** and **14**, all these compounds have similar R_1 group but different R_2 groups (Table-1). On the basis of IC_{50} value, compound **14** was more active as compare to **9**, **10** and **11**. The docking results showed that compound **14** interacted with three active site residues (Asn241, Arg312 and Phe300) as compare to compound **9** which interacted with only two active site residues (Asn241 and Arg312) (Figure-7 and 5b). The increase biological activity of compound **14** might be due to the interaction with more active site residues as compare to compound **9**. The difference in the activities and binding modes of these compounds might be attributed by the different R_2 groups present in these compounds.

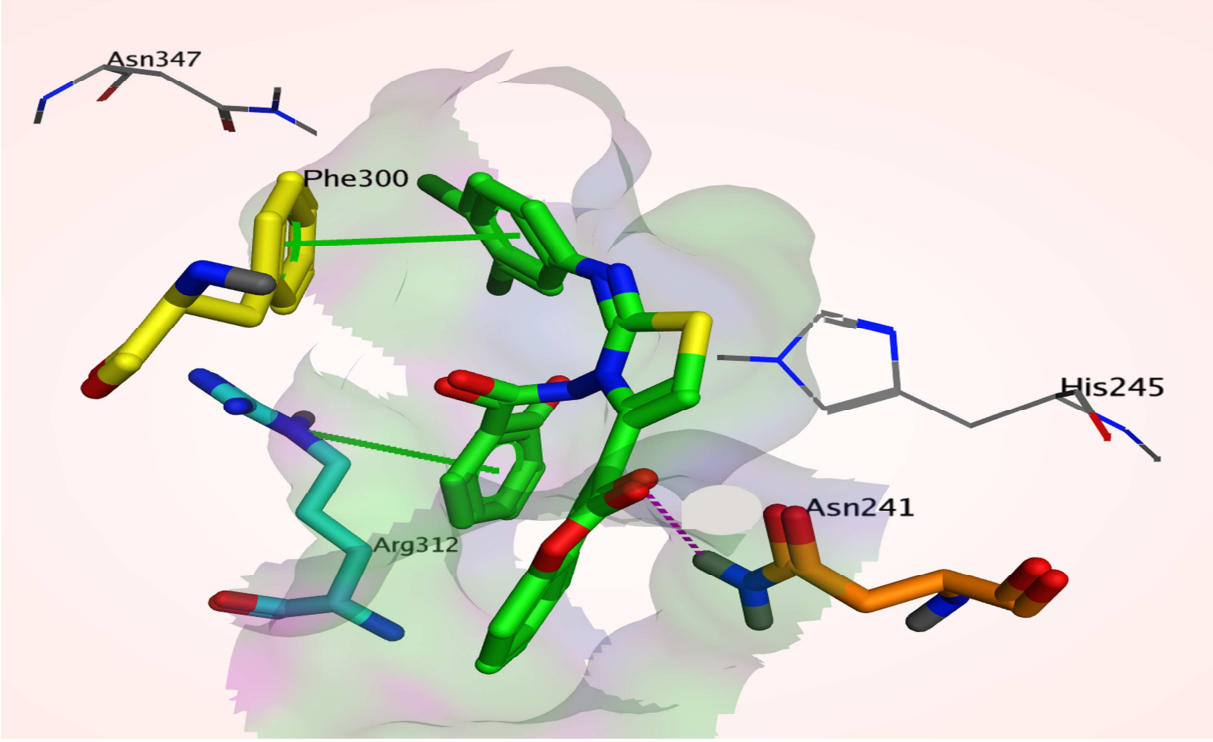


Figure-7: Docked conformer of the compound **14** and its interactions with the residues of the *α*-glucosidase protein.

From the biological activity and molecular docking studies of these compounds, we have experienced that compounds having electron rich centers at one end and electron withdrawing or electronegative centers at the other end were responsible for adequate α-glucosidase inhibitory activity.

Conclusion

3-Thiazolylcoumarin derivatives **1-14** were found to have superior *in vitro* α-glucosidase inhibitory activity in the range of IC_{50} = 0.12 ± 0.01-16.20 ± 0.23 μM as compared to standard acarbose (IC_{50} = 38.25 ± 0.12 μM). Molecular docking study was carried out in order to get insights about the molecular interaction of compounds with the active site of enzyme. Superior activity of compounds suggest that these may serve as lead molecules for further research for getting powerful α-glucosidase inhibitors.

Experimental

Materials and Methods

Analytical grade reagents and solvents were purchased from Sigma-Aldrich and used as received. Thin layer chromatography was performed on pre-coated silica gel, GF-254. Spots were visualized under ultraviolet light at 254 and 366 nm. Mass spectra were recorded under electron impact (EI) on MAT 312 and MAT 113D mass spectrometer. The ^{1}H- and ^{13}C-NMR were recorded on Bruker AM spectrometer, operating at 300, 400 and 500 MHz instruments. 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.

In Vitro α-Glucosidase Inhibition Assay

α-Glucosidase inhibitory potential of all synthetic 3-thiazolylcoumarin derivatives were checked by reported method [52]. Typically, α-glucosidase activity was performed in phosphate buffer 50 mM of pH 6.8 which contains 5% v/v dimethyl sulfoxide. PNP glycoside was used as a substrate. The inhibitors were pre-incubated with enzyme for half an hour at 37 $^{\circ}$C. Then substrate was added and the enzymatic reaction was performed for 60 min at 37 $^{\circ}$C. Absorbances were measured by spectrophotometer at 400 nm. The assay was carried in triplicate with five

different concentrations around the IC_{50} values that were calculated in the first turn of the experiments, and the mean values were adopted.

Protein Model Preparation

The sequence of the target protein (α-glucosidase) was retrieved from the uniprot in FASTA format and protein-blast [53] was carried to get its template in protein databank [54]. The 3D crystal structures of the template Pdb Id: 3A47 A was retrieved from the protein databank.

Homology Modeling

First the sequence in FASTA format was copied and pasted in the sequence editor of the MOE (Molecular Operating Environment) software and in MOE window the 3D structure of the template protein was opened. Chain1 and chain2 showed the target and template protein sequences, respectively. RMSD value of target-template sequences was calculated prior to homology modeling. In model refining tool Intermediate was set to Medium, Final model to Medium, using scoring function Generalized Born/Volume Integral (GB/VI). The Force field was set to Amber99 with Salvation RField. Total of 30 models were generated, and the final refine model was loaded to MOE window.

General Experimental Procedure for the Syntheses of 3-Thiazolylcoumarin Derivatives 1-14

Substituted benzohydrazide derivative (1 mmol), substituted benzene isothiocyanate (1 mmol) were taken in ethanol (10 mL) into a 100 mL round-bottomed flask were refluxed for half an hour. Intermediate formation was carefully monitored by thin layer chromatography (TLC). After the consumption of both starting materials 3-(bromoacetyl) coumarin (1 mmol) and trimethylamine (1 mmol) were added into above mixture and further refluxed for 3 h. TLC was taken in order to check the reaction progress. After completion of reaction, reaction mixture was poured onto about 100 g crushed ice. Precipitates were formed which were filtered to get crude products which were crystallized from ethyl acetate to afford pure products in high yields.

(*Z*)-4-Methoxy-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (1)

Dark green solid; Yield: 72%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.33 (s, 1H, NH), 8.76 (s, 1H, H-4), 7.81 (d, $J_{2''',3'''/6''',5'''}$ = 8.8 Hz, 2H, H-2''', 6'''), 7.51 (d, $J_{2'',3''/6'',5''}$ = 8.8 Hz, 3H, H-5, 2'', 6''), 7.30 (t, $J_{7,6}$ = $J_{7,8}$ = 6.8 Hz, 1H, H-7), 7.12 (d, $J_{3''',2'''/5''',6'''}$ = 8.8 Hz, 2H, H-3''', 5'''), 7.03 (d, $J_{8,7}$ = 9.2 Hz, 1H, H-8), 6.94 (d, $J_{3'',2''/5'',6''}$ = 9.2 Hz, 2H, H-3'', 5''), 6.90 (t, $J_{6,7}$ = $J_{6,7}$ = 8.8 Hz, 1H, H-8), 4.76 (s, 1H, 5'), 3.82 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.6, 159.1, 159.0, 158.2, 155.8, 154.1, 153.2, 141.1, 130.4, 128.4, 128.4, 128.1, 127.8, 125.6, 125.2, 124.1, 122.0, 122.0, 118.2, 116.0, 115.2, 115.2, 114.3, 114.3, 100.2, 55.7, 55.5; Anal. Calcd for $C_{27}H_{21}N_3O_5S$, C = 64.92, H = 4.24, N = 8.41; Found C = 64.90, H = 4.26, N = 8.44; EI MS *m/z* (% rel. abund.): 499 (M^+ , 2), 457 (30), 429 (5), 326 (21), 313 (100), 297 (72); HRMS (EI) calcd for $C_{27}H_{21}N_3O_5S$: *m/z* = 499.1202, found 499.1182.

(*Z*)-*N*-(2-((4-Methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (2)

Dark green solid; Yield: 80%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.41 (s, 1H, NH), 8.80 (s, 1H, H-4), 7.88 (m, 1H, H-5), 7.56 (m, 4H, H-2''', 3''', 5''', 6'''), 7.36 (m, 4H, H-8, 3'', 5''), 6.95 (d, $J_{2'',3''/6'',5''}$ = 9.2 Hz, 2H, H-2'', 6''), 6.87 (m, 3H, H-6, 7, 4'''), 3.70 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.6, 159.3, 159.0, 158.2, 155.7, 153.1, 141.2, 132.0, 132.0, 130.4, 128.7, 128.7, 128.2, 127.8, 127.3, 127.3, 125.6, 125.2, 122.1, 122.1, 118.0, 116.2, 115.1, 115.1, 100.2, 55.7; Anal. Calcd for $C_{26}H_{19}N_3O_4S$, C = 66.51, H = 4.08, N = 8.95; Found C = 66.53, H = 4.06, N = 8.97; EI MS *m/z* (% rel. abund.): 470 (M^+ , 2), 456 (100), 441 (66), 427 (9), 410 (3), 386 (3), 364 (18), 336 (6); HRMS (EI) calcd for $C_{26}H_{19}N_3O_4S$: *m/z* = 469.9096, found 469.9092.

(*Z*)-2,4-Dimethoxy-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (3)

Dark green solid; Yield: 76%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.25 (s, 1H, NH), 8.83 (s, 1H, H-4), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 8.0 Hz, 1H, H-7), 7.65 (d, $J_{5,6}$ = 8.4 Hz, 1H, H-5), 7.51 (d, $J_{2'',3''/6'',5''}$ = 9.2 Hz, 2H, H-2'', 6''), 6.94 (d, $J_{3'',2''/5'',6''}$ = 8.8 Hz, 2H, H-3'', 5''), 6.89 (m, 2H, H-6, 8), 6.79 (d, $J_{6''',5'''}$ = 8.8 Hz, 1H, H-6'''), 6.73 (bd.s, 1H, H-3'''), 6.69 (d, $J_{5''',6'''}$ = 8.4 Hz, 1H, H-5'''), 4.89 (s, 1H, H-5'), 3.86 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.7, 163.1, 159.3, 159.2, 158.2, 155.7, 153.1, 141.2, 136.3, 130.4, 129.3, 128.4, 127.7, 125.8, 125.3, 122.0, 122.0, 118.2, 116.3, 115.2, 115.2, 110.4, 110.2, 100.0, 98.2, 55.8, 55.8,

55.6; Anal. Calcd for $C_{28}H_{23}N_3O_6S$, C = 63.51, H = 4.38, N = 7.93; Found C = 63.53, H = 4.36, N = 7.91; EI MS *m/z* (% rel. abund.): 529 (M^+ , 4), 496 (18), 467 (3), 401 (5), 356 (4), 343 (16); HRMS (EI) calcd for $C_{28}H_{23}N_3O_6S$: *m/z* = 529.1308, found 529.1280.

(*Z*)-*N*-(2-((4-Methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)-2,4-dimethylbenzamide (4)

Dark green solid; Yield: 78%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.37 (s, 1H, NH), 8.83 (s, 1H, H-4), 8.00 (d, $J_{6''',5'''}$ = 6.0 Hz, 1H, H-6'''), 7.78 (t, $J_{6,5}$ = $J_{6,7}$ = 6.0 Hz, 1H, H-6), 7.66 (d, $J_{5,6}$ = 6.4 Hz, 1H, H-5), 7.52 (d, $J_{2'',3''/6'',5''/5''',6'''}$ = 6.8 Hz, 3H, H-2'', 6'', 5'''), 7.49 (s, 1H, H-4), 7.45 (t, $J_{7,6/7,8}$ = 6.0 Hz, 1H, H-7), 7.22 (s, 1H, 3'''), 7.19 (d, $J_{8,7}$ = 6.4 Hz, 1H, H-8), 6.94 (d, $J_{3'',2''/5'',6''}$ = 6.8 Hz, 2H, H-3'', 5''), 4.89 (s, 1H, H-5'), 3.72 (s, 3H, OCH_3), 2.56 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.7, 159.3, 159.0, 158.4, 155.7, 153.1, 141.2, 138.1, 137.0, 132.2, 131.2, 130.3, 128.4, 127.8, 127.4, 126.0, 125.6, 125.2, 122.0, 122.0, 118.2, 116.0, 115.1, 115.1, 100.2, 55.6, 21.7, 19.4; Anal. Calcd for $C_{28}H_{23}N_3O_4S$, C = 67.59, H = 4.66, N = 8.45; Found C = 67.57, H = 4.63, N = 8.47; EI MS *m/z* (% rel. abund.): 497 (M^+ , 9), 470 (10), 372 (24), 358 (20), 350 (44); HRMS (EI) calcd for $C_{28}H_{23}N_3O_4S$: *m/z* = 497.1409, found 497.1403.

(*Z*)-3,5-Dimethoxy-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (5)

Dark green solid; Yield: 74%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ8.76 (s, 1H, H-4), 8.00 (d, $J_{5,6}$ = 7.6 Hz, 1H, H-5), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 7.2 Hz, 1H, H-7), 7.51 (d, $J_{8,7}$ = 8.4 Hz, 1H, H-8), 7.46 (t, $J_{6,5}$ = $J_{6,7}$ = 7.2 Hz, 1H, H-6), 7.34 (d, $J_{2'',3''/6'',5''}$ = 8.8 Hz, 1H, H-2'',6''), 7.06 (d, $J_{3'',2''/5'',6''}$ = 8.8 Hz, 1H, H-3'',5''), 6.50 (s, 1H, H-2''', 4''', 6'''), 4.79 (s, 1H, H-5'), 3.77 (s, 3H, OCH_3),3.61 (s, 6H, $2OCH_3$); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.8, 161.5, 161.5, 159.3, 159.0, 158.2, 155.8, 153.1, 141.2, 136.1, 130.6, 128.4, 127.8, 125.6, 125.2, 122.2, 122.2, 118.3, 116.0, 115.2, 115.2, 105.3, 105.3, 103.9, 100.0, 55.9, 55.7, 55.7; Anal. Calcd for $C_{28}H_{23}N_3O_6S$, C = 63.51, H = 4.38, N = 7.93; Found C = 63.53, H = 4.40, N = 7.90; EI MS *m/z* (% rel. abund.): 529 (M^+ , 2), 487 (40), 459 (5), 372 (14), 356 (19), 342 (100); HRMS (EI) calcd for $C_{28}H_{23}N_3O_6S$: *m/z* = 529.1308, found 529.1305.

(*Z*)-2-Methoxy-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (6)

Dark green solid; Yield: 81%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.33 (s, 1H, NH), 8.75 (s, 1H, H-4), 7.73 (d, $J_{5,6}$ = 7.6 Hz, 1H, H-5), 7.53 (m, 4H, H-7, 2'', 6'', 4'''), 7.23 (d, $J_{8,7}$ = $J_{6''',5'''}$ = 8.0 Hz, 2H, H-8, 6'''), 7.11 (t, $J_{7,6}$ = $J_{7,8}$ = 7.2 Hz, 1H, H-7), 6.94 (d, $J_{3'',4''/5'',6''}$ = 8.8 Hz, 2H, H-3'', 5''), 6.89 (bd.m, 2H, H-3''', 5'''), 3.87 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.7, 159.3, 159.0, 158.2, 157.4, 155.7, 153.1, 141.2, 133.2, 131.8, 130.3, 128.2, 127.7, 125.6, 125.2, 122.2, 122.0, 121.0, 118.3, 118.1, 116.2, 115.1, 115.1, 111.3, 100.2, 55.8, 55.6; Anal. Calcd for $C_{27}H_{21}N_3O_5S$, C = 64.92, H = 4.24, N = 8.41; Found C = 64.90, H = 4.26, N = 8.39; EI MS *m/z* (% rel. abund.): 499 (M^+ , 2), 475 (2), 456 (6), 441 (4), 371 (27), 364 (17), 297 (100); HRMS (EI) calcd for $C_{27}H_{21}N_3O_5S$: *m/z* = 499.1202, found 499.1185.

(*Z*)-4-(*tert*-Butyl)-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (7)

Dark green solid; Yield: 72%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ8.77 (s, 1H, H-4), 8.00 (d, $J_{5,6}$ = 7.2 Hz, 1H, H-5), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 7.2 Hz, 1H, H-7), 7.51 (d, $J_{8,7}$ = 8.4 Hz, 1H, H-8), 7.46 (t, $J_{6,5}$ = $J_{6,7}$ = 7.2 Hz, 1H, H-6), 7.37 (m, 6H, H-2'', 3'', 5'', 6'', 2''', 6'''), 7.05 (d, $J_{3''',2'''/5''',6'''}$ = 8.8 Hz, 2H, H-3''',5'''), 4.78 (s, 1H, H-5'), 3.77 (s, 3H, OCH_3), 1.22 (s, 9H, 3OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.7, 159.3, 159.0, 158.2, 155.7, 154.6, 153.1, 141.2, 130.4, 128.8, 128.2, 127.7, 127.0, 127.0, 125.6, 125.3, 125.1, 125.1, 122.2, 122.2, 118.3, 116.0, 115.2, 115.2, 100.3, 55.7, 34.0, 31.2, 31.2, 31.2; Anal. Calcd for $C_{30}H_{27}N_3O_4S$, C = 68.55, H = 5.18, N = 7.99; Found C = 68.52, H = 5.15, N = 7.97; EI MS *m/z* (% rel. abund.): 523 (M^+ , 6), 483 (62), 468 (9), 455 (11), 352 (34), 339 (75), 324 (100); HRMS (EI) calcd for $C_{30}H_{27}N_3O_4S$: *m/z* = 525.1722, found 525.1692.

(*Z*)-4-Bromo-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (8)

Dark green solid; Yield: 77%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.44 (s, 1H, NH), 8.76 (s, 1H, H-4), 7.79 (m, 2H, H-3'', 5''), 7.58 (d, $J_{5,6}$ = 8.4 Hz, 1H, H-5), 7.52 (m, 2H, H-2''', 6'''), 7.33 (m, 3H, H-6, 7, 8), 7.05 (d, $J_{2'',3''/6'',5''}$ = 8.8 Hz, 2H, H-2'', 6''), 6.95 (d, $J_{3'',2''/5'',6''}$ = 8.8 Hz, 2H, H-3'',5''),

4.80 (s, 1H, H-5'), 3.72 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.7, 159.3, 159.0, 158.1, 155.7, 153.2, 141.1, 131.5, 131.5, 131.1, 130.4, 129.8, 129.8, 128.2, 127.7, 125.4, 126.3, 125.1, 122.3, 122.3, 118.2, 116.0, 115.1, 115.1, 100.2, 55.6; Anal. Calcd for $C_{26}H_{18}BrN_3O_4S$, C = 56.94, H = 3.31, N = 7.66; Found C = 56.92, H = 3.34, N = 7.64; EI MS *m/z* (% rel. abund.): 547 (M^+, 2), 549 (M+2, 2), 505 (23), 479 (5), 376 (19), 363 (50), 347 (22), 329 (37); HRMS (EI) calcd for $C_{26}H_{18}BrN_3O_4S$: *m/z* = 547.0201, found 547.0192.

(*Z*)-2-Hydroxy-*N*-(2-((4-methoxyphenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (9)

Dark green solid; Yield: 80%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.24 (s, 1H, NH), 8.77 (s, 1H, H-4), 8.01 (d, $J_{5,6}$ = 8.0 Hz, 1H, H-5), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 7.6 Hz, 1H, H-7), 7.51 (d, $J_{8,7}$ = 8.4 Hz, 1H, H-8), 7.46 (t, $J_{6,5}$ = $J_{6,7}$ = 7.6 Hz, 1H, H-6), 7.25 (m, 3H, H-2", 6", 4'''), 7.11 (d, $J_{6''',5'''}$ = 7.6 Hz, 1H, H-6'''), 6.98 (d, $J_{3'',2''/5'',6''}$ = 8.8 Hz, 2H, H-3", 5"), 6.81 (d, $J_{3''',4'''}$ = 8.0 Hz, 1H, H-3'''), 6.77 (d, $J_{5''',4'''}$ = $J_{5''',6'''}$ = 7.2 Hz, 1H, H-5'''), 4.81 (s, 1H, H-5'), 3.73 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.6, 159.3, 159.2, 159.0, 158.1, 155.7, 153.1, 141.4, 133.4, 130.3, 128.7, 128.5, 127.7, 125.8, 125.5, 122.0, 122.0, 121.2, 119.7, 118.3, 117.7, 116.2, 115.1, 115.1, 100.2, 55.9; Anal. Calcd for $C_{26}H_{19}N_3O_5S$, C = 64.32, H = 3.94, N = 8.65; Found C = 64.30, H = 3.91, N = 8.63; EI MS *m/z* (% rel. abund.): 458 (M^+, 52), 443 (38), 415 (5), 312 (100), 299 (35), 266 (58); HRMS (EI) calcd for $C_{26}H_{19}N_3O_5S$: *m/z* = 485.1045, found 485.1036.

(*Z*)-*N*-(2-((3-Bromophenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)-3,5-dimethoxybenzamide (10)

Dark green solid; Yield: 69%; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 10.20 (s, 1H, NH), 8.79 (s, 1H, H-4), 8.03 (d, $J_{5,6}$ = 8.0 Hz, 1H, H-5), 7.82 (t, $J_{7,6}$ = $J_{7,8}$ = 8.5 Hz, 1H, H-7), 7.53 (d, $J_{8,7}$ = 8.5 Hz, 1H, H-8), 7.48 (t, $J_{6,5}$ = $J_{6,7}$ = 7.5 Hz, 1H, H-6), 7.25 (m, 3H, H-2", 6", 4'''), 7.19 (d, $J_{3'',2''/5'',6''}$ = 8.8 Hz, 2H, H-3", 5"), 7.16 (d, $J_{6''',5'''}$ = 7.5 Hz, 1H, H-6'''), 6.80 (m, 2H, H-3''', 5'''), 4.85 (s, 1H, H-5'), 2.28 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.7, 159.3, 159.1, 158.5, 155.8, 153.1, 146.2, 136.7, 133.3, 130.6, 130.4, 130.4, 128.7, 128.1, 127.8, 125.9, 125.3, 121.2, 119.7, 119.7, 119.7, 118.2, 117.6, 116.2, 100.3, 21.5; Anal. Calcd for $C_{27}H_{20}BrN_3O_5S$, C = 56.06, H = 3.49, N = 7.26; Found C = 56.04, H = 3.47, N = 7.29; EI MS *m/z* (% rel. abund.): 577 (M^+, 2), 579 (M+2

, 1.8),451 (12), 436 (8), 360 (12); HRMS (EI) calcd for $C_{27}H_{20}BrN_3O_5S$: *m/z* = 577.0307, found 577.0301.

(*Z*)-*N*-(2-((3-Bromophenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)-2-hydroxybenzamide (11)

Dark green solid; Yield: 75%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.04 (s, 1H, NH), 8.76 (s, 1H, H-4), 8.01 (d, $J_{5,6}$ = 8.0 Hz, 1H, H-5), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 7.6 Hz, 1H, H-7), 7.63 (m, 2H, H-2", 4"), 7.51 (d, $J_{8,7}$ = 8.4 Hz, 1H, H-8), 7.46 (t, $J_{6,5}$ = $J_{6,7}$ = 7.6 Hz, 1H, H-6), 7.41 (t, $J_{4''',3'''}$ = 8.0 Hz, 1H, H-4'''), 7.31 (d, $J_{6''',5'''}$ = 8.4 Hz, 1H, H-6'''), 7.26 (m, 2H, H-5", 6"), 6.83 (d, $J_{5''',4'''}$ = $J_{5''',6'''}$ =7.6 Hz, 1H, H-5'''), 6.79 (d, $J_{3''',4'''}$ = 8.4 Hz, 1H, H-3'''), 4.83 (s, 1H, H-5'); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.6, 159.3, 159.0, 158.4, 155.7, 153.2, 151.1, 133.7, 130.4, 130.1, 128.8, 128.4, 127.8, 125.6, 125.2, 125.0, 123.7, 123.2, 121.5, 121.3, 119.7, 118.2, 117.9, 116.3, 100.2; Anal. Calcd for $C_{25}H_{16}BrN_3O_4S$, C = 56.19, H = 3.02, N = 7.86; Found C = 56.17, H = 3.04, N = 7.89; EI MS *m/z* (% rel. abund.): 533 (M^+ , 25), 535 (M+2, 27), 493 (7), 386 (6), 362 (19), 347 (100), 317 (5); HRMS (EI) calcd for $C_{25}H_{16}BrN_3O_4S$: *m/z* = 533.0045, found 533.0027.

(*Z*)-*N*-(2-((3,4-Dichlorophenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)-2,4-dimethoxybenzamide (12)

Dark green solid; Yield: 68%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ10.92 (s, 1H, NH), 8.82 (s, 1H, H-4), 7.93 (d, $J_{2'',6''}$ = 2.4 Hz, 1H, H-2"), 7.68 (d, $J_{6'',5''/6''',5'''}$ = 8.4 Hz, 2H, H-6", 6'''), 7.61 (d, $J_{5'',6''/5''',6'''}$ = 8.8 Hz, 2H, H-5", 5'''), 7.51 (m, 3H, H-5, 7, 8), 6.74 (bd.s, 1H, H-3'''), 6.70 (d, $J_{6,5}$ = 8.0 Hz, 1H, H-6), 4.88 (s, 1H, H-5'), 3.88 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ164.6, 163.1, 159.5, 158.2, 155.8, 153.2, 148.4, 136.6, 131.7, 131.6, 131.0, 130.6, 129.6, 128.4, 127.8, 125.6, 125.5, 120.7, 120.6, 118.3, 116.2, 110.4, 110.2, 100.2, 98.4, 55.8, 55.6; Anal. Calcd for $C_{27}H_{19}Cl_2N_3O_5S$, C = 57.05, H = 3.37, N = 7.39; Found C = 57.07, H = 3.34, N = 7.41; EI MS *m/z* (% rel. abund.): 538 (M^+-OMe, 2), 388 (12), 365 (43), 313 (35); HRMS (EI) calcd for $C_{27}H_{19}Cl_2N_3O_5S$: *m/z* = 567.0422, found 567.0418.

(*Z*)-4-(*tert*-Butyl)-*N*-(2-((3,4-dichlorophenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)benzamide (13)

Dark green solid; Yield: 65%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.10 (s, 1H, NH), 7.95 (bd.s, 1H, H-2''), 7.84 (d, $J_{2''',3'''/6''',5'''}$ = 8.0 Hz, 2H, H-2''', 6'''), 7.68 (m, 9H, H-4, 5, 6, 7, 8, 5'', 6'', 3''', 5'''), 4.81 (s, 1H, H-5'), 1.31 (s, 9H, 3CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.7, 159.5, 158.4, 155.7, 154.8, 153.2, 148.6, 131.7, 131.6, 131.2, 130.6, 128.7, 128.2, 127.8, 127.2, 127.2, 125.7, 125.5, 125.2, 125.2, 120.5, 120.3, 118.3, 116.0, 100.2, 34.1, 31.4, 31.4, 31.4; Anal. Calcd for $C_{29}H_{23}Cl_2N_3O_3S$, C = 61.71, H = 4.11, N = 7.44; Found C = 61.74, H = 4.13, N = 7.42; EI MS *m/z* (% rel. abund.): 563 (M^+ , 2), 565 (M+2, 2), 405 (9), 390 (19), 362 (35), 346 (17), 330 (26), 218 (35); HRMS (EI) calcd for $C_{29}H_{23}Cl_2N_3O_3S$: *m/z* = 563.0837, found 563.0834.

(*Z*)-*N*-(2-((3,4-Dichlorophenyl)imino)-4-(2-oxo-2*H*-chromen-3-yl)thiazol-3(2*H*)-yl)-2-hydroxybenzamide (14)

Dark green solid; Yield: 70%; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.98 (s, 1H, NH), 8.76 (s, 1H, H-4), 8.00 (d, $J_{5,6}$ = 7.2 Hz, 1H, H-7), 7.80 (t, $J_{7,6}$ = $J_{7,8}$ = 7.2 Hz, 1H, H-7), 7.71 (m, 2H, H-2'', 6''), 7.51 (d, $J_{8,7}$ = 8.4 Hz, 1H, H-8), 7.46 (t, $J_{5,6}$ = 7.6 Hz, 1H, H-5), 7.30 (m, 3H, H-5'', 4''', 6'''), 6.86 (t, $J_{5''',4'''}$ = $J_{5''',6'''}$ =7.2 Hz, 1H, H-5'''), 6.77 (d, $J_{3''',4'''}$ = 8.4 Hz, 1H, H-3'''), 4.81 (s, 1H, H-5'); ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.8, 159.5, 159.3, 158.2, 155.7, 153.1, 148.4, 133.6, 131.8, 131.4, 131.0, 130.6, 128.8, 128.4, 127.9, 125.6, 125.3, 121.5, 120.7, 120.4, 119.7, 118.0, 117.8, 116.2, 100.2; Anal. Calcd for $C_{25}H_{15}Cl_2N_3O_4S$, C = 57.26, H = 2.88, N = 8.01; Found C = 57.23, H = 2.86, N = 8.03; EI MS *m/z* (% rel. abund.): 523 (M^+ , 37), 495 (7), 481 (25), 453 (6), 350 (90), 337 (53), 304 (58), 288 (12); HRMS (EI) calcd for $C_{25}H_{15}Cl_2N_3O_4S$: *m/z* = 523.0160, found 523.0152.

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Research Highlights

- Synthesis of new 3-thiazolylcoumarin
- Hybrid of thiazole and coumarin
- α-Glucosidase inhibitory properties
- Molecular docking studies were carried out
- Useful in diabetic complications