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ORIGINAL ARTICLE

Synthesis, in vitro α-glucosidase inhibitory activity, and in silico study of (*E*)-thiosemicarbazones and (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives

Muhammad Ali[1] · Khalid Mohammed Khan[1,3] · Uzma Salar[1] · Mohammed Ashraf[2] · Muhammad Taha[3] · Abdul Wadood[4] · Sujhla Hamid[2] · Muhammad Riaz[4] · Basharat Ali[1] · Shahbaz Shamim[1] · Farman Ali[1] · Shahnaz Perveen[5]

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Abstract
This study is focused on the identification of thiazole-based inhibitors for the α-glucosidase enzyme. For that purpose, (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives were synthesized in two steps and characterized by various spectroscopic techniques. All derivatives and intermediates were evaluated for their in vitro α-glucosidase inhibitory activity. Thiosemicarbazones **20** and **35**, and cyclized thiazole derivatives **2**, **5**–**11**, **13**, **15**, **21**–**24**, **27**–**31**, and **36**–**37** showed significant inhibitory potential in the range of $IC_{50} = 6.2 \pm 0.19$–43.6 ± 0.23 μM as compared to standard acarbose ($IC_{50} = 37.7 \pm 0.19$ μM). A molecular modeling study was carried out to understand the binding interactions of compounds with the active site of enzyme.

Keywords Synthesis · In vitro · α-glucosidase · Structure–activity relationship (SAR) · In silico

Introduction

Diabetes mellitus is a serious metabolic disorder of modern era and severe interminable health complications are associated with it, and type-2 diabetes is widely spread kind of this disorder [1]. The α-glucosidase enzyme is necessary for human physiological function, but its overexpression increases glucose level in plasma [2] after a meal. This enzyme is present in the cell membrane of the small intestine [3,4] and it is responsible for the digestion of carbohydrates (polysaccharides) into simple absorbable monosaccharides [5,6]. The inhibition of α-glucosidase restricts the production of glucose which is helpful in the treatment of diabetes [7]. Since 1980, the number of people in the world with diabetes increased from 153 to 347 million in 2008 [8]. According to WHO, it is expected that diabetes would be the seventh driving reason for death universally by 2030 [9].

Acarbose, miglitol, and voglibose are clinically used drugs and these all are α-glucosidase inhibitors [10]. Unfortunately, gastrointestinal tract side effects such as diarrhea, flatulence, and abdominal discomfort are associated with them. Moreover, these are 50% less effective than other classes of antidiabetic agents such as metformin and sulfonylurea [11,12] and frequently used in combination with other antidiabetic drugs to improve efficacy. Therefore, it is a crucial need to develop new, safe, and efficient therapeutic agents to control the optimal glycemic index for curing type-2 diabetic patients.

Thiazole, or 1,3-thiazole, is a heterocyclic compound that possesses both sulfur and nitrogen atoms [13]. Thiazole is an

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✉ Khalid Mohammed Khan
khalid.khan@iccs.edu; drkhalidhej@gmail.com

1 H. E. J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi 75270, Pakistan

2 Department of Biochemistry and Biotechnology, The Islamia University of Bahawalpur, Bahawalpur 63100, Pakistan

3 Department of Clinical Pharmacy, Institute for Research and Medical Consultations (IRMC), Imam Abdulrahman Bin Faisal University, P.O. Box 31441, Dammam, Saudi Arabia

4 Department of Biochemistry, Shankar Campus, Abdul Wali Khan University, Mardan, Khyber Pukhtoonkhwa, Pakistan

5 PCSIR Laboratories Complex, Karachi, Shahrah-e-Dr. Salimuzzaman Siddiqui, Karachi 75280, Pakistan

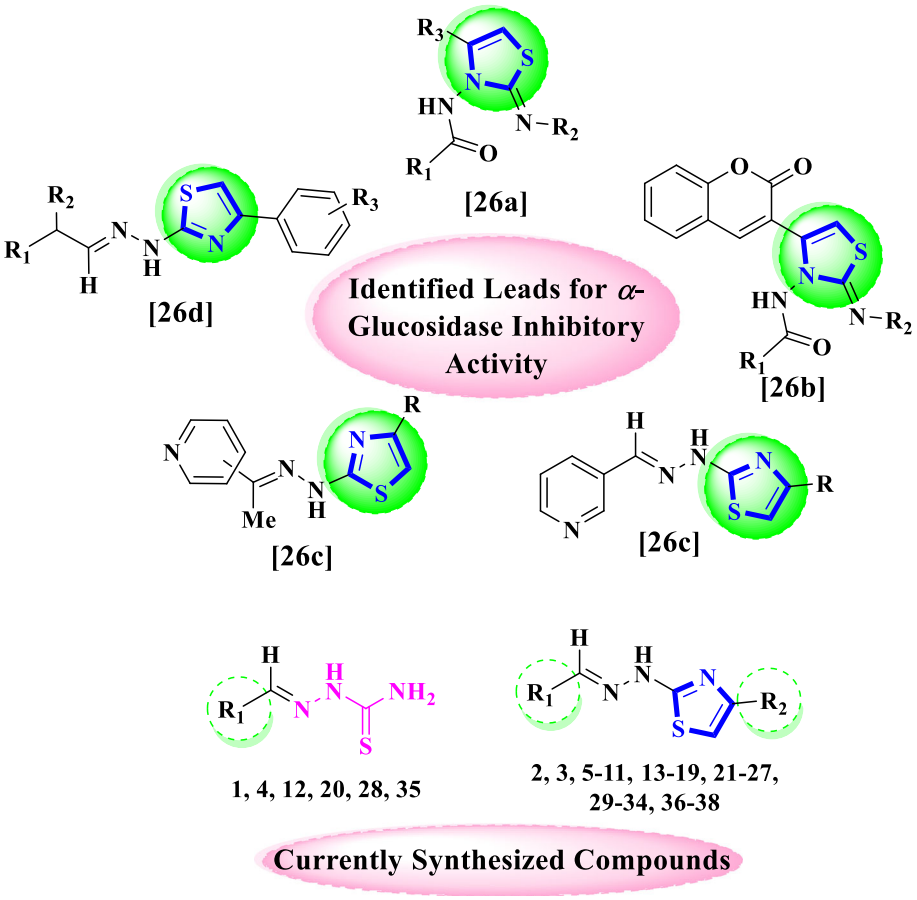


Fig. 1 Rationale of current study

aromatic compound that obeys the Hückel rule [14]. The thiazole heterocycle can exist in two isomeric forms, 1,3-thiazole often considered as thiazole or 1,2-thiazole also known as isothiazole [15]. Thiazole-containing molecules are used in CNS disorders [16], and showed anticancer, antimalarial [17], as well as antiviral activities against four viruses such as polio, influenza A (H1N1), hepatitis B and hepatitis C [18]. In addition to these biological activities, thiazole derivatives such as thiamethoxam and clothianidin play a pivotal role as insecticides in many crop-protecting agrochemicals [19].

Our research group has identified a number of lead candidates based on heterocyclic nucleus for their use in medicinal chemistry research [20–25] and found thiazole-based compounds as potential α-glucosidase inhibitors (Fig. 1) [13,26].

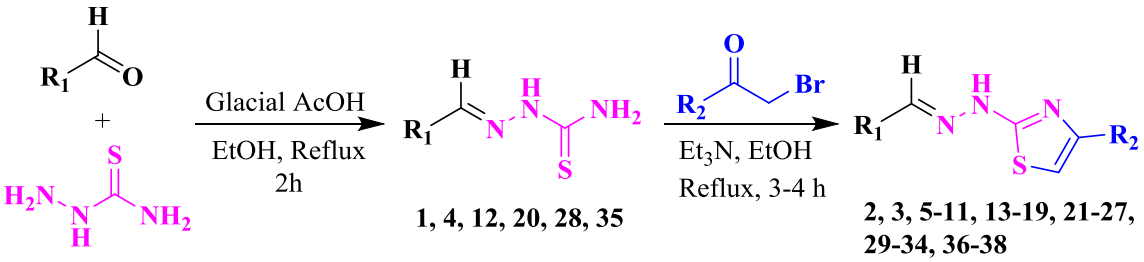
In the current study, we intended to further evaluate this class for α-glucosidase inhibitory activity. Thus, this report presents the synthesis of (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives along with the thiosemicarbazone intermediates (**1**–**38**), structural characterization, their α-glucosidase inhibitory activity, and *in silico* studies.

Results and discussion

Chemistry

(*E*)-2-(2-(Arylmethylene)hydrazinyl)-4-arylthiazole derivatives were synthesized by a two-step reaction route. In the first step, different aryl aldehydes were reacted with thiosemicarbazide in the presence of few drops of glacial acetic acid to form the thiosemicarbazones **1**, **4**, **12**, **20**, **28**, and **35**. In second step, these thiosemicarbazones were treated with a variety of phenacyl bromides in the presence of triethyl amine to afford hydrazinyl thiazoles **2**, **3**, **5**–**11**, **13**–**19**, **21**–**27**, **29**–**34**, and **36**–**38**. Progress of both steps was monitored by thin layer chromatography (TLC) (Scheme 1).

The identity of all compounds was confirmed by EI-MS, HREI-MS, ^{1}H- and ^{13}C-NMR spectroscopic techniques. 2D-NMR experiments such as COSY, HSQC, and HMBC were performed on intermediate **1** and cyclized derivative **6** to further confirm the exact framework of the compounds. The stereochemistry of the iminic double bond was confirmed by the NOESY analysis on intermediate **1** and cyclized derivative **6**. In both cases, NOESY interaction was observed between NH and iminic carbon of the compounds which can only be observed in an *E*-configuration (Fig. 2).



Scheme 1 Synthesis of (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives

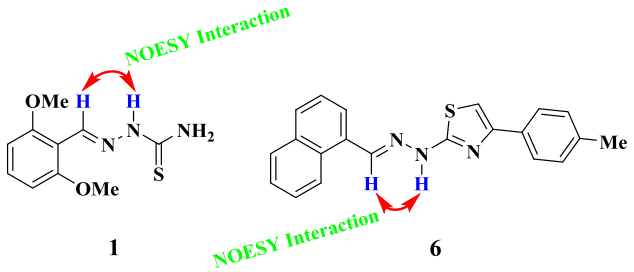


Fig. 2 NOESY interaction between NH and iminic carbon

In vitro α-glucosidase inhibitory activity

(*E*)-2-(2-(Arylmethylene)hydrazinyl)-4-arylthiazole derivatives along with intervening thiosemicarbazones (**1–38**) were subjected to in vitro α-glucosidase inhibitory activity testing. Compounds **2**, **5–11**, **13**, **15**, **20–24**, **27–31**, and **35–37** showed inhibitory activity in the range of $IC_{50} = 6.2 \pm 0.19$–43.6 ± 0.23 μM versus that of standard acarbose ($IC_{50} = 37.7 \pm 0.19$ μM) (Table 1).

Structure–activity relationship (SAR)

All molecules possess biologically important pharmacophores such as hydrazine and thiazole moieties those might be participating in the inhibitory activity. But molecules also possess varying groups such as R_1 and R_2 (Fig. 3). Thus, a limited SAR was rationalized by examining the effects of varying features (R_1 and R_2) on inhibitory potential.

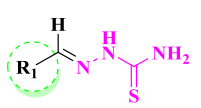
Thiosemicarbazone **1** did not show α-glucosidase inhibition; however, its cyclized products compound **2** ($IC_{50} = 37.3 \pm 0.17$ μM) with *p*-methoxy substitution displayed α-glucosidase inhibitory activity comparable to standard acarbose ($IC_{50} = 37.7 \pm 0.19$ μM). Interestingly, *m*-nitro containing analog **3** was found to be completely inactive. Its inactivity is might be due to not fulfilling the conformational requirement to fit well in the active site of the enzyme (Fig. 4).

1-Naphthyl-substituted thiosemicarbazone **4** was found to be inactive. The inactivity of this compound might be due to the presence of naphthyl ring which may create steric hindrance while binding into the active site of α-glucosidase enzyme. All cyclized analogs **6–11** were found to be inhibitors for the α-glucosidase enzyme except compound **5** with unsubstituted phenyl ring as R_2. Among them, compound **8** ($IC_{50} = 6.2 \pm 0.19$ μM) with a biphenyl group as R_2 was found to be the most potent molecule. Its activity might be due to the extended π-system which can interact with active site of α-glucosidase enzyme. Replacement of phenyl ring with bromo group at the *para* position of R_2 as in compound **10** ($IC_{50} = 7.9 \pm 0.19$ μM) showed slight decreased α-glucosidase inhibitory activity. Nonetheless, replacement with *p*-methoxy and *m*-nitro groups as in compounds **7** ($IC_{50} = 12.2 \pm 0.20$ μM) and **9** ($IC_{50} = 13.6 \pm 0.20$ μM), respectively, also showed decrease inhibitory potential as compared to compound **8**. Compound **11** ($IC_{50} = 26.1 \pm 0.20$ μM) with *m*,*p*-dichloro substitution showed better activity when compared to standard acarbose, but activity was lower than compounds **7–10**. Relatively decreased activity might be attributed due to two chloro atoms adjacent to each other which may create steric hindrance while binding into the active site of enzyme. Similarly, compound **6** ($IC_{50} = 38.5 \pm 0.18$ μM) with *p*-methyl substitution showed comparable activity to standard acarbose. The pattern for α-glucosidase inhibitory activity on the basis of R_2 was observed in the order of *p*-Ph > unsubstituted > *p*-Br > *p*-OMe > *p*-NO_2 > *m*, *p*-*di*Cl > *p*-Me (Fig. 5).

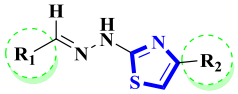
2-Naphthyl-substituted thiosemicarbazone **12** along with cyclized derivatives **14**, and **16–19** were found to be inactive for α-glucosidase inhibitory activity; however, compounds **13** ($IC_{50} = 28.4 \pm 0.23$ μM) with no substitution and **15** ($IC_{50} = 37.2 \pm 0.22$ μM) with *p*-methoxy substitutions on R_2 were found to be good inhibitors for α-glucosidase enzyme (Fig. 6).

Naphthol-substituted thiosemicarbazone **20** ($IC_{50} = 21.5 \pm 0.21$ μM) and its cyclized hydrazinyl thiazoles **21–27** demonstrated α-glucosidase inhibitory activity. Among them, compound **21** ($IC_{50} = 7.3 \pm 0.19$ μM) with no substitution on R_2, was found to be the most potent derivative. Incorporation of groups such as methyl, methoxy, and phenyl at the *para* position of R_2 as in compounds **22** ($IC_{50} = 27.5 \pm 0.21$ μM), **23** ($IC_{50} = 18.2 \pm 0.21$ μM), and **24** ($IC_{50} = 35.4 \pm 0.22$ μM) led to decreased activity. It showed that *para* position is not participating in the inhibitory

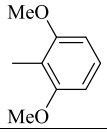
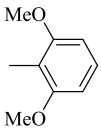
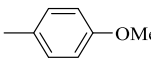
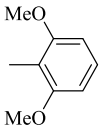
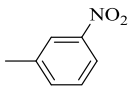
Table 1 In vitro α-glucosidase inhibitory activity and calculated docking scores of synthesized compounds (**1-38**)



1, 4, 12, 20, 28, 35



2, 3, 5-11, 13-19, 21-27, 29-34, 36-40

Compounds	R_1	R_2	α-Glucosidase inhibitory activity	
			$IC_{50} \pm SEM^a$ (μM)	Docking Score (kcal/mol)
Category "A"				
1		-	NA[b]	-6.47
2			37.3 ± 0.17	-12.02
3			NA[b]	-8.85
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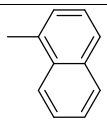
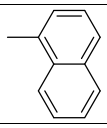
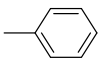
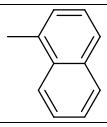
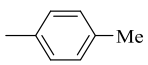
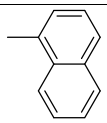
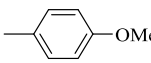
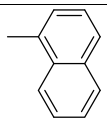
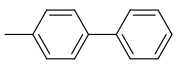
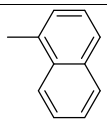
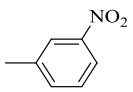
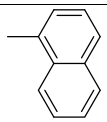
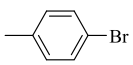
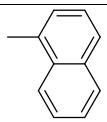
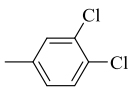
4		-	NA[b]	-7.71
5			7.4 ± 0.19	-15.59
6			38.5 ± 0.18	-11.46
7			12.2 ± 0.20	-14.11
8			6.2 ± 0.19	-16.05
9			13.6 ± 0.20	-13.72
10			7.9 ± 0.19	-15.38
11			26.1 ± 0.22	-12.70

Table 1 continued

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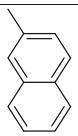
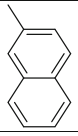
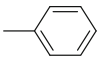
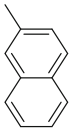
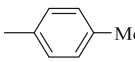
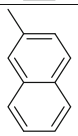
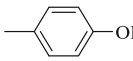
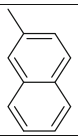
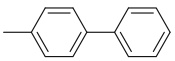
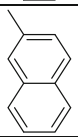
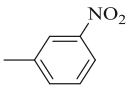
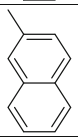
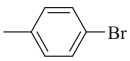
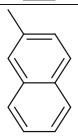
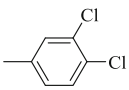
12		-	NA[b]	-8.43
13			28.4 ± 0.23	-12.23
14			NA[b]	-7.37
15			37.2 ± 0.22	-11.64
16			NA[b]	-7.77
17			NA[b]	-6.42
18			NA[b]	-7.46
19			NA[b]	-7.71
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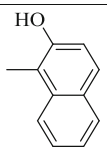
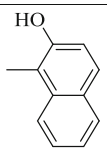
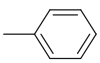
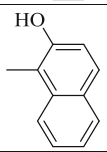
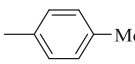
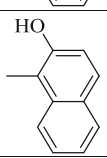
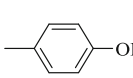
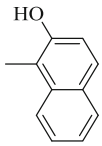
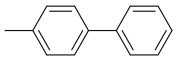
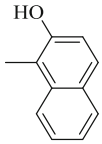
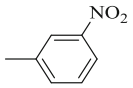
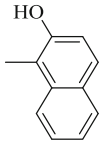
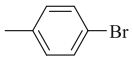
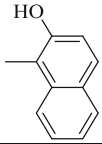
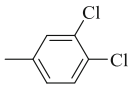
20		-	21.5 ± 0.21	-12.86
21			7.3 ± 0.19	-15.48
22			27.5 ± 0.21	-12.13
23			18.2 ± 0.21	-13.33

Table 1 continued

24			35.4 ± 0.22	-11.72
25			NA[b]	-10.52
26			NA[b]	-11.01
27			18.6 ± 0.24	-12.93
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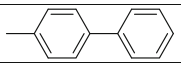
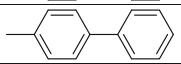
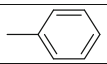
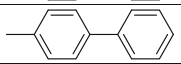
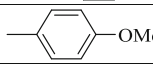
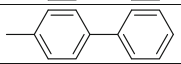
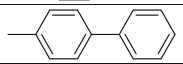
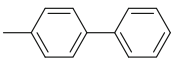
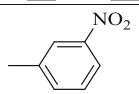
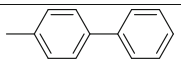
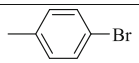
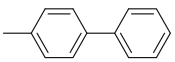
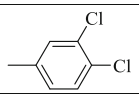
28		-	39.6 ± 0.23	-11.43
29			27.7 ± 0.21	-12.03
30			16.3 ± 0.21	-13.60
31			38.2 ± 0.23	-11.68
32			NA[b]	-7.33
33			NA[b]	-7.02
34			NA[b]	-8.01
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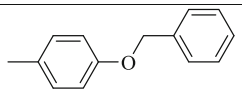
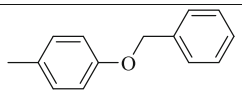
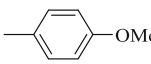
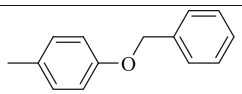
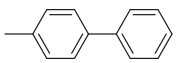
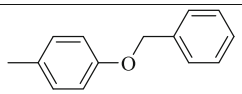
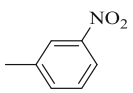
35		-	17.9 ± 0.26	-13.08
36			41.6 ± 0.23	-10.38
37			43.6 ± 0.23	-10.11
38			NA[b]	-6.63
Standards	**Acarbose[c]**		37.7 ± 0.19	

[a] SEM (Standard error mean); [b] NA (Not active; compounds demonstrated < 50% inhibition); Acarbose[c] (Standard inhibitor for α-glucosidase inhibitory activity)

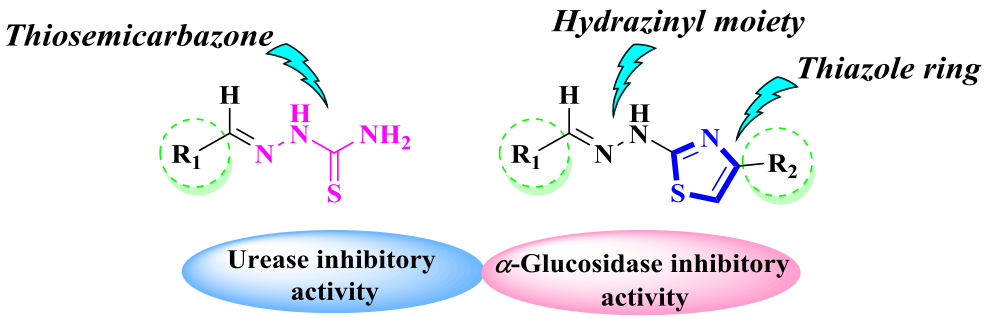


Fig. 3 General features of synthesized compounds

Fig. 4 Structure–activity relationship of compounds **1–3**

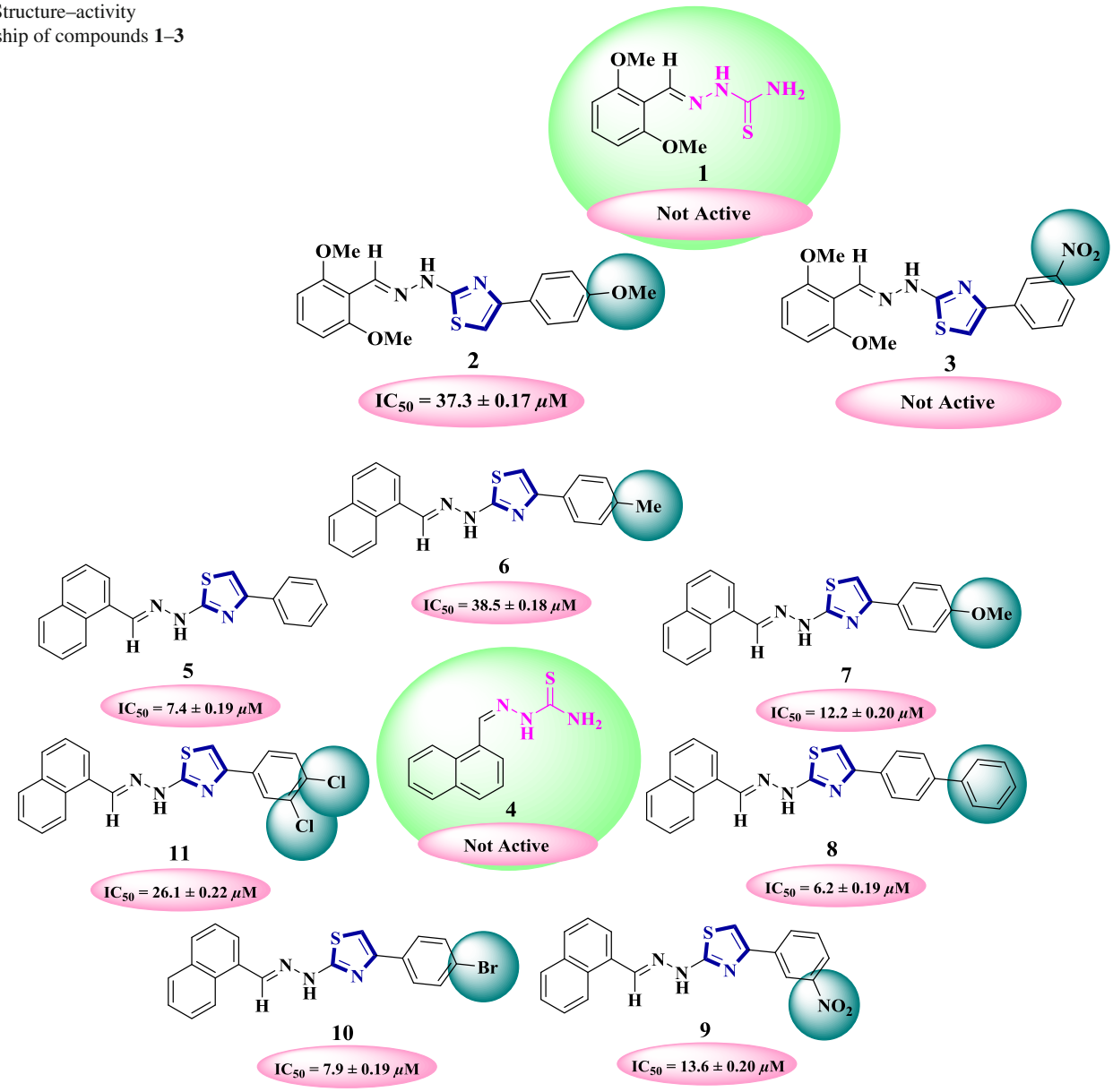


Fig. 5 Structure–activity relationship of compounds **4–11**

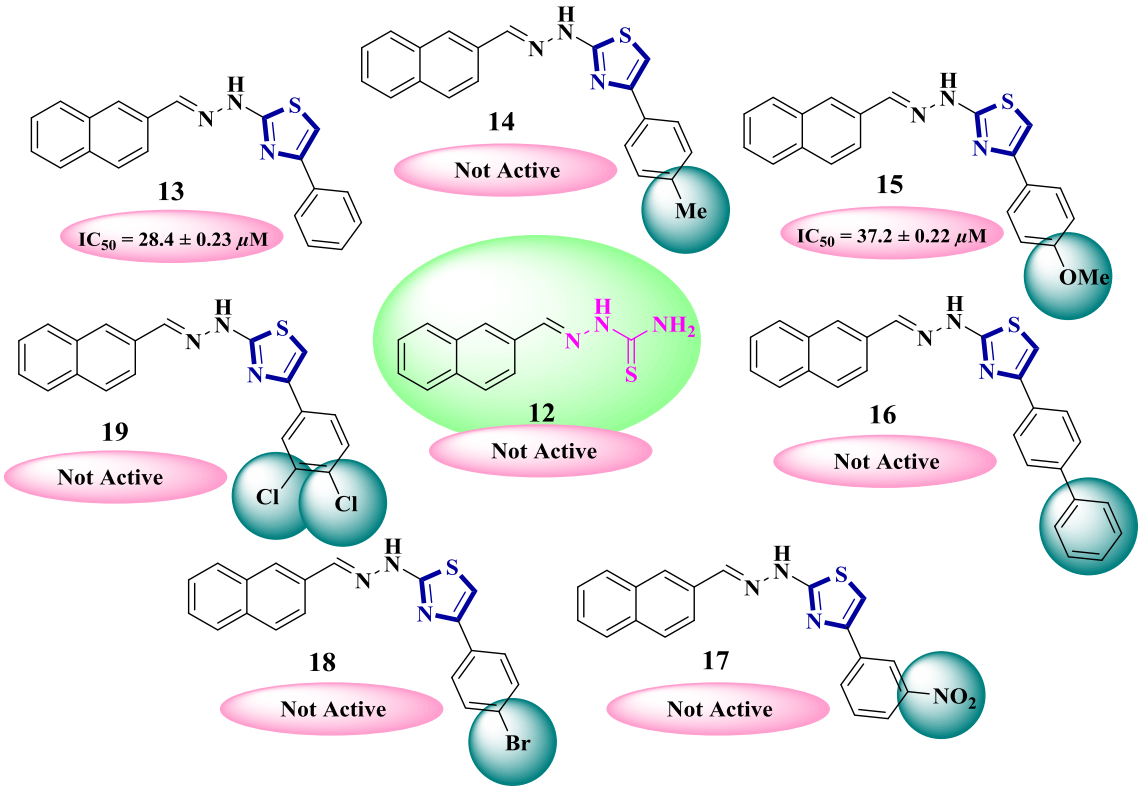


Fig. 6 Structure–activity relationship of compounds **12–19**

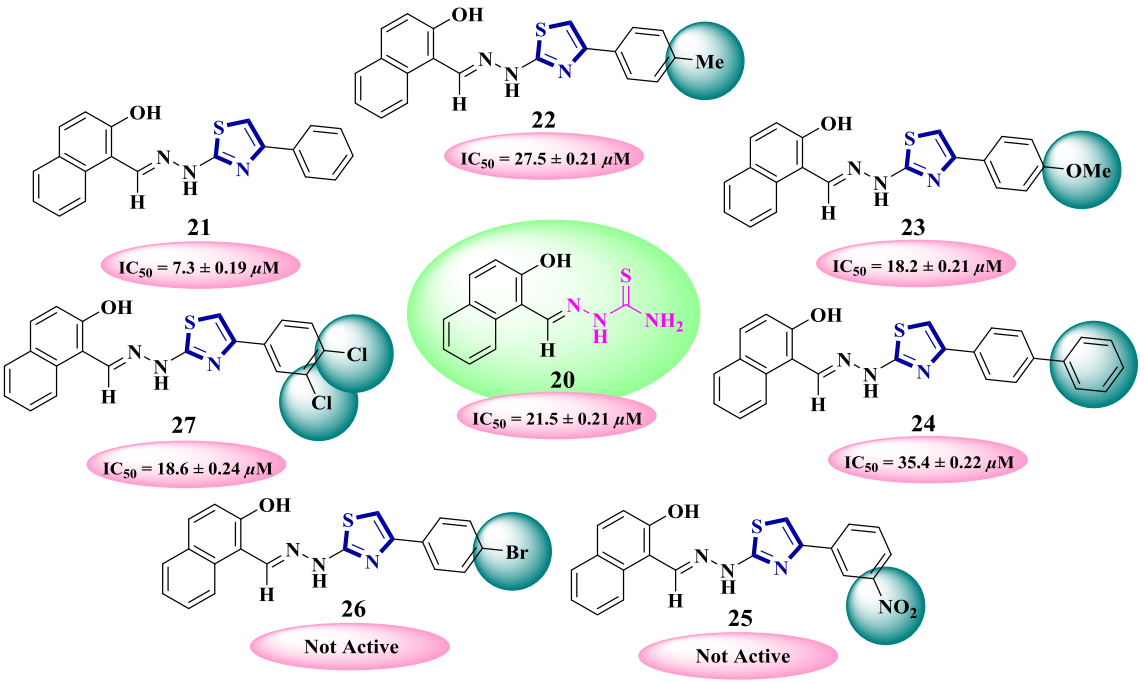


Fig. 7 Structure–activity relationship of compounds **20–27**

potential. Similarly, compound **27** ($IC_{50} = 18.6 \pm 0.24\ \mu M$) with *m*,*p*-dichloro atoms was also found to be less active than unsubstituted analog **21**. The pattern of α-glucosidase inhibitory activity was found in the order of unsubstituted > *p*-OMe > *m*,*p*-*di*Cl > *p*-Me > *p*-Ph > *p*-Br ~ *p*-NO_2 (Fig. 7).

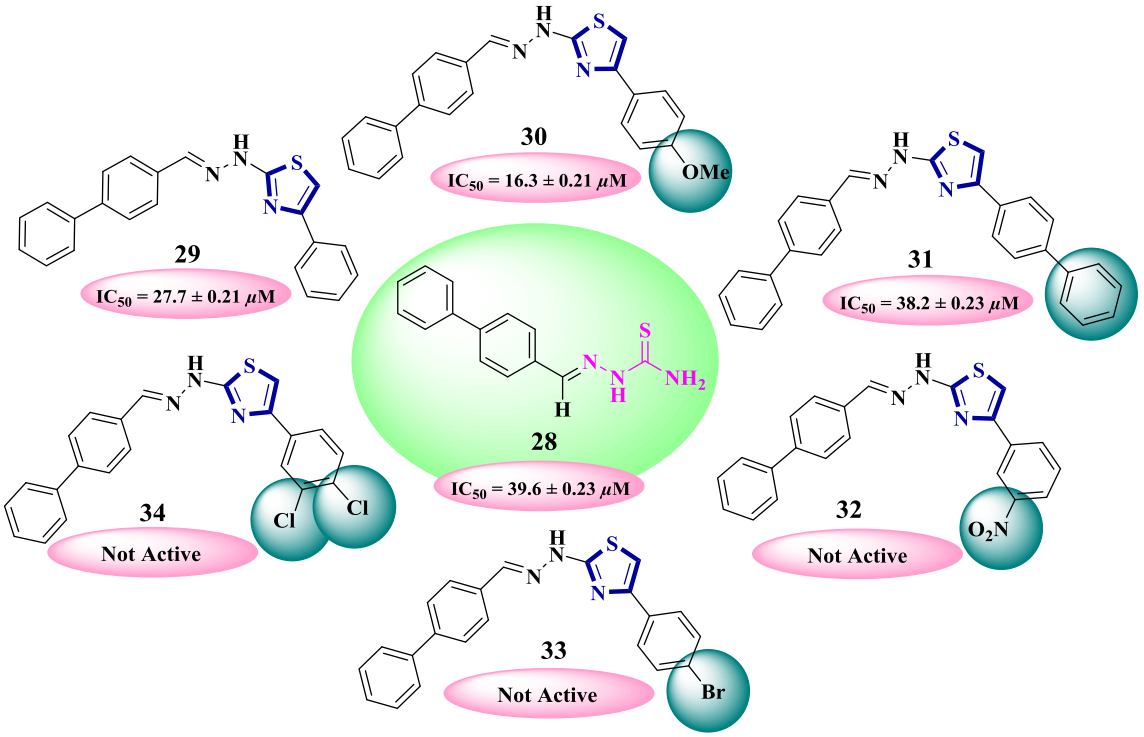


Fig. 8 Structure–activity relationship of compounds **28–34**

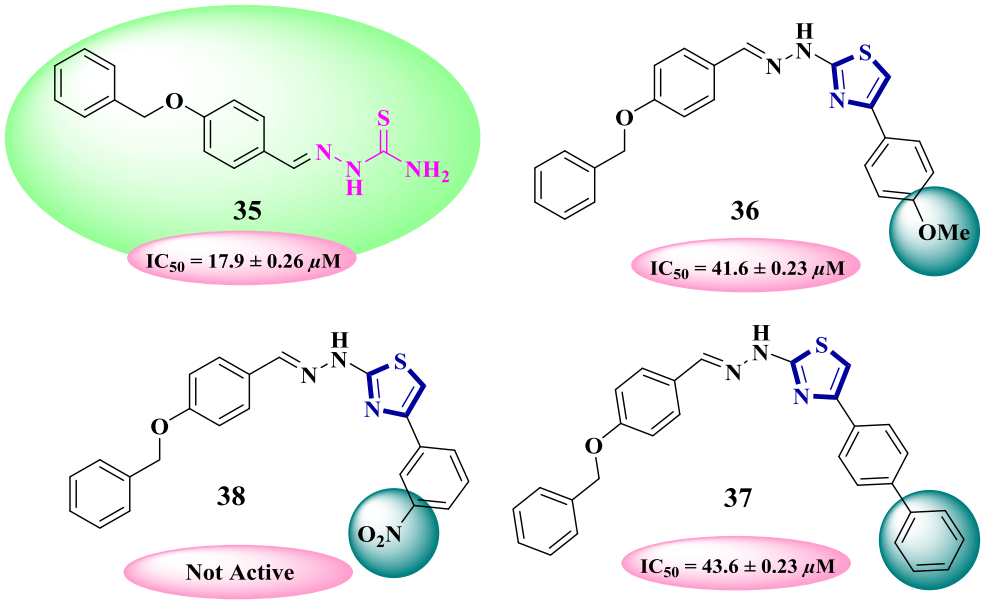


Fig. 9 Structure–activity relationship of compounds **35–40**

Biphenyl thiosemicarbazone **28** and its cyclized compounds **29–31** showed potential toward the inhibition of α-glucosidase enzyme. Compound **30** (IC_{50} = 16.3 ± 0.21 μM) with *p*-methoxy substitution was found to be the most potent analog when compared to unsubstituted derivative **29** (IC_{50} = 27.7 ± 0.21 μM). Comparison of compound **30** with **31** revealed that replacing the methoxy group with the phenyl ring in compound **31** (IC_{50} = 38.2 ± 0.23 μM), leads to further decreased inhibitory activity which shows that methoxy group is playing an important role in the activity (Fig. 8).

4-Benzyloxy benzylidene thiosemicarbazone **35** (IC_{50} = 17.9 ± 0.26 μM) and its cyclized hydrazinyl thiazole derivative **36** (IC_{50} = 41.6 ± 0.23 μM) with *p*-methoxy and **37**

($IC_{50} = 43.6 \pm 0.23$ μM) with *p*-Ph substitutions showed α-glucosidase inhibitory activity comparable to standard acarbose (Fig. 9).

Overall, most of the thiosemicarbazones, except for **20** and **35**, were failed to show α-glucosidase enzyme. It is worth mentioning that most of the cyclized hydrazinyl thiazole derivatives showed α-glucosidase inhibitory activity. However, in order to further evaluate the participation of various structural features in the interactions with the active site of enzyme, a molecular docking study was conducted as discussed below.

Molecular docking study

Preparation of the synthesized derivatives

To predict the binding mode of the synthesized (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives with α-glucosidase enzyme, a molecular docking study was carried out using MOE (Molecular Operating Environment) software package [29]. The three-dimensional structures of the synthesized derivatives were generated by using the builder tool in MOE. The generated compounds were 3D protonated and energy minimized using the default parameters of MOE (gradient: 0.05, Force Field: MMFF94X). All the compounds were then saved into an mdb file for further evaluation.

Preparation of α-glucosidase 3D structure

The 3D structure for α-glucosidase of *Saccharomyces cerevisiae* has not been solved yet; however, several homologies models of α-glucosidase have been reported [30–33]. In this study, we used our reported 3D homology model of α-glucosidase of *Saccharomyces cerevisiae* [34].

For docking studies, the parameters of MOE used were: Placement: Triangle Matcher, Rescoring 1: London dG, Refinement: Forcefield, Rescoring 2: GBVI/WSA. For each ligand 10 conformations were allowed to be formed and on the basis of docking score the top ranked conformations were selected for further analysis. Docking score is the binding free energy calculated by the GBVI/WSA scoring function which is the score of the last stage showing the overall stability of the predicted complex. For all scoring functions, lower scores indicate more favorable poses. The calculated docking scores for α-glucosidase enzyme are listed in Table 1 and the unit for all scoring functions is kcal/mol.

Interactions detail

All synthetic derivatives **1**–**38** that were divided into six different categories, i.e., A, B, C, D, E and F on the basis of their geometries, were docked into the binding pocket of α-glucosidase enzyme in order to find the binding interactions of the compounds within the active-site residues. On the basis of docking scores, the best conformations were analyzed for hydrogen bonding/arene-arene/arene-cation interactions, at the end of docking experiment. Similarly, various degrees of inhibitory potentials were predicted for the active derivatives of the series against α-glucosidase enzyme.

Figure 10a–d presents the binding mode of some most active compounds. For example, Fig. 10a shows that compound **5** fits well into the binding cavity of α-glucosidase enzyme showing three interactions with residues Phe177, Asn347, and Arg312. Phe177 participates in π–H interaction with the arylthiazole π-electron system. Asn347 forms another π–H interaction with the π-electrons of arylthiazole. Similarly, Arg312 forms a third π–H bond with the π-electrons of arylhydrazinyl group.

Compound **7** in this group is an intermediary active compound which forms two noticeable interactions with the binding site residues Phe177 and Glu304 as presented in Fig. 10b. Phe177 shows π–H interaction with the arylhydrazinyl ring of compound.

A side chain H-donor interaction was also perceived between Glu304 and H of the thiazole group. Figure 10c shows the binding mode of the most active compound **8**, forming four important interactions with active site residues His279, Asn241, and Phe177. His279 forms a polar interaction with the S of thiazole and a π–H bond with hydrazinyl group of compound.

Asn347 involves a side chain H-acceptor interaction with the nitrogen of hydrazinyl group and Phe177 shows π–H interaction with the arylhydrazinyl group. Compound **10** is another significantly active compound in this group and shows two different interactions with the residues Glu276 and Phe157 as shown in Fig. 10d. Glu276 establishes an H-donor interaction with the Br of arylthiazole group. A second strong H-donor bond is observed between Phe157 and hydrazinyl group. The 3D binding mode also shows that Asp408 may also form another H-donor bond with the S of thiazole moiety as the distance between them was measured as 2.86 Å. In addition to the catalytic residues, molecular docking studies of (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives predict that residues like Phe157, Asn347, Arg312, Glu304, and His279 have an important role in the α-glucosidase inhibition.

Conclusion

Synthetic (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazoles along with intermediates were screened for α-glucosidase inhibitory activity. A number of compounds demonstrated good inhibitory potential. Molecular model-

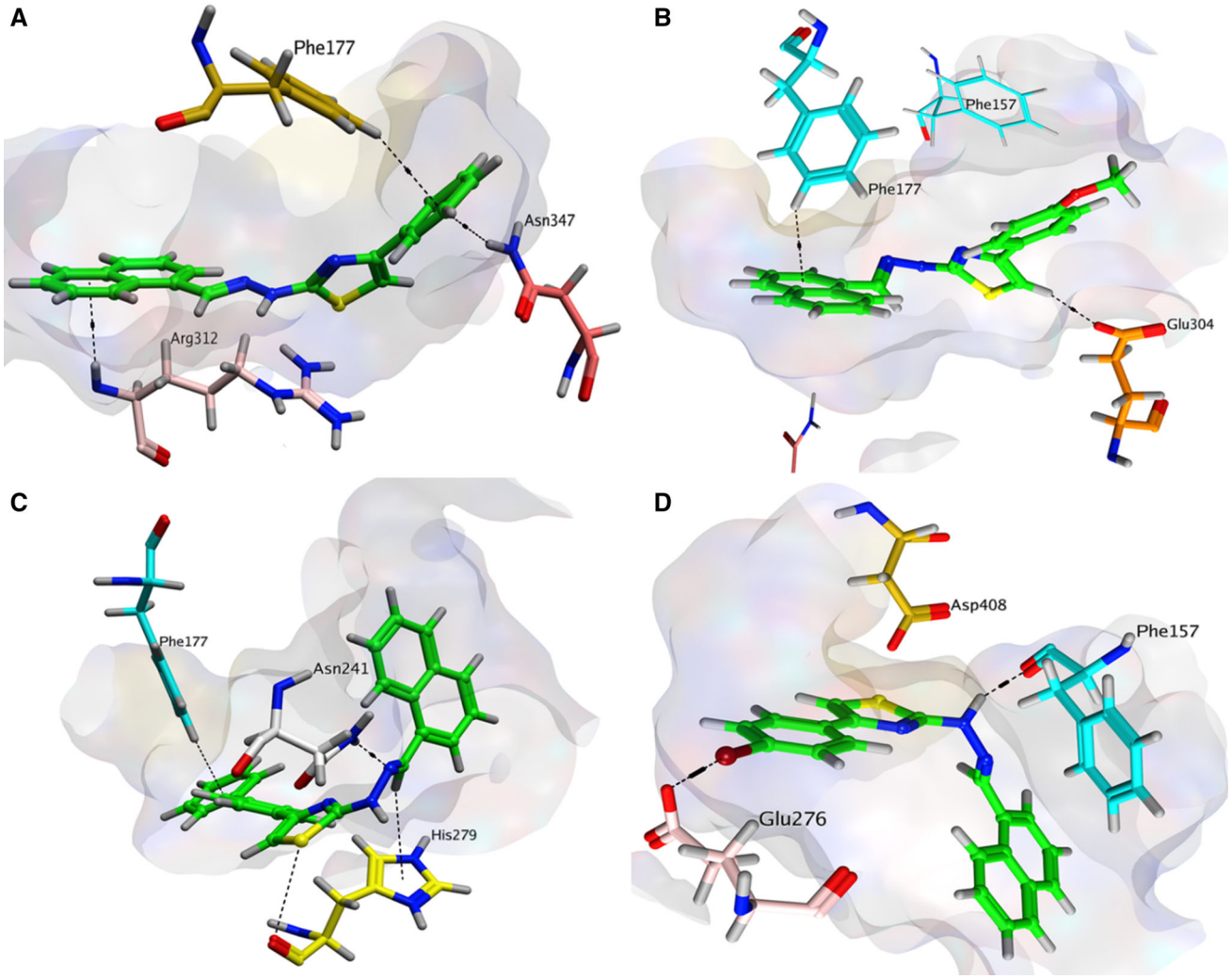


Fig. 10 Docking conformations of compounds in α-glucosidase enzyme. **a** 3D binding mode of compound **5**. **b** 3D binding mode of compound **7**. **c** 3D binding mode of compound **8**. **d** 3D binding mode of compound **10**. Ligands are shown green

ing identified structural features that participate in binding interactions with the active sites of enzyme. This study identified a number of promising candidates that may serve as leads for the future research in search of therapeutic agents for type-2 diabetes mellitus.

Experimental

Materials and methods

Reagents were purchased from Sigma-Aldrich (USA) and were of analytical grade. 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) condition on Varian Massen Spectrometers MAT 312 and MAT 113D. The ^{1}H-NMR and ^{13}C-NMR were recorded on Bruker AM machines operating at 300, 400 and 500 MHz. Chemical shift values are presented in ppm (δ) relative to tetramethylsilane (TMS) as an internal standard and the coupling constant (J) are in Hz. Multiplicities are reported as singlet (s), doublet (d), triplet (t), doublet of doublets (dd), doublet of triplets (dt), quartet (q) or multiplet (m).

General procedure for the synthesis of thiosemicarbazone intermediates (1, 4, 12, 20, 28, 35)

Different aryl aldehydes (10 mmol) and thiosemicarbazide (10 mmol) were taken in ethanol (50 mL) into a 250-mL round-bottomed flask with few drops of glacial acetic acid.

The reaction mixture was refluxed for 4 h with constant stirring. Progress of reaction was monitored by thin-layer chromatography (TLC). After completion, the resulting precipitate was filtered and washed with 10 mL cold ethanol to afford the pure product in good yields. All compounds **1**, **4**, **12**, **20**, **28**, **35** were characterized by the spectroscopic techniques. To the best of our knowledge, structures of all intermediates are known [35–40].

(*E*)-2-(2,6-Dimethoxybenzylidene) hydrazinecarbothioamide (1) [35]

Solid; Light orange; Yield: 73%; M.P.: 182–184 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1H, NH), 8.29 (s, 1H, H–C=N), 8.09 (s, 1H, NH), 7.33 (t, $J_{4(3,5)}$ = 8.4 Hz, 1H, H-4), 7.19 (s, 1H, NH), 6.69 (d, $J_{3,4}$ = $J_{5,4}$ = 8.4 Hz, 2H, H-3, H-5), 3.78 (s, 6H, 2OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6):δ 177.7 (C=S), 158.8 (C-2), 158.8 (C-6), 138.2 (HC=N), 131.2 (CH-4), 110.3 (C-1), 104.3 (CH-3), 104.3 (CH-5), 56.0 (OCH_3), 56.0 (OCH_3); EI-MS m/z (% rel. abund.): 239 (M^+, 95), 164 (83), 163 (89), 149 (100), 121 (51), 106 (67), 91(95), 51(88); HREI-MS Calcd for $C_{10}H_{13}N_3O_2S$: m/z = 239.0728, found 239.0730; Anal. Calcd for $C_{10}H_{13}N_3O_2S$: C = 50.19; H = 5.48; N = 17.56; Found: C = 50.21; H = 5.50; N = 17.59.

(*E*)-2-(Naphthalen-1-ylmethylene)hydrazine-carbothioamide (4) [36]

Solid; White; Yield: 78%; M.P.: 119-121 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 8.90 (s, 1H, H–C=N), 8.36 (d, $J_{2,3}$ = 8.4 Hz, 1H, H-2), 8.25 (s, 1H, NH), 8.21 (d, $J_{4,3}$ = 6.8 Hz, 1H, H-4), 8.00 (d, $J_{5,6}$ = $J_{8,7}$ = 8.4 Hz, 2H, H-5, H-8), 7.95 (s, 1H, NH), 7.66 (t, $J_{3(2,4)}$ = 8.0 Hz, 1H, H-3), 7.59 (overlapping multiplet, 2H, H-6, H-7); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 177.8 (C=S), 142.6 (HC=N), 133.7 (C-10), 130.5 (CH-4), 130.3 (C-9), 128.7 (CH-5), 128.2 (C-1), 127.8 (CH-3), 126.4 (CH-6), 126.4 (CH-7), 125.7 (CH-2), 123.2 (CH-8); EI-MS m/z (% rel. abund.): 229 (M^+, 77), 195 (17), 169 (44), 154 (86), 153 (100), 127 (47); HREI-MS Calcd for $C_{12}H_{11}N_3S$:m/z = 229.0674, found 229.0670; Anal. Calcd for $C_{12}H_{11}N_3S$:C = 62.86; H = 4.84; N = 18.33; Found: C = 62.84; H = 4.83; N = 18.31.

(*E*)-2-(Naphthalen-2-ylmethylene) hydrazinecarbothioamide (12) [37]

Solid; Off white; Yield: 67%; M.P.: 132–134 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 8.22 (s, 1H, H-1), 8.20 (s, 1H, H–C=N), 8.17 (d, $J_{3,4}$ = 8.7 Hz, 1H, H-3), 8.10 (s, 1H, H-NH), 8.07 (bd s, 1H, NH), 7.96 (overlapping multiplet, 3H, H-4, H-5, H-8), 7.55 (dd, $J_{6,8}$ = $J_{7,5}$ = 3.0 Hz, $J_{6,5}$ = $J_{7,8}$ = 6 Hz, 2H, H-6, H-7); ^{13}C-NMR (125 MHz, DMSO-d_6):δ 177.6 (C=S), 145.9 (HC=N), 136.2 (C-10), 132.7 (C-9), 129.3 (C-2), 128.3 (CH-4), 128.0 (CH-1), 127.7 (CH-8), 127.5 (CH-5), 127.3 (CH-3), 126.3 (CH-6), 126.1 (CH-7); EI-MS m/z (% rel. abund.): 229 (M^+, 68), 212 (10), 195 (21), 169 (23), 153 (100), 127 (44), 115 (19); HREI-MS Calcd for $C_{12}H_{11}N_3S$: m/z = 229.0674, found 229.0671; Anal. Calcd for $C_{12}H_{11}N_3S$: C = 62.86; H = 4.84; N = 18.33; Found: C = 62.87; H = 4.86; N = 18.35.

(*E*)-2-((2-Hydroxynaphthalen-1-yl) methylene) hydrazinecarbothioamide (20) [38]

Solid; Light yellow; Yield: 75%; M.P.: 271–273 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.35 (s, 1H, NH), 9.03 (s, 1H, H–OH), 8.50 (d, $J_{8,7}$ = 8.1 Hz, 1H, H-8), 8.19 (s, 1H, H–C=N), 7.88 (overlapping multiplet, 4H, H-4, H-5, 2NH), 7.57 (m, 1H, H-7), 7.39 (t, $J_{6(5,7)}$ = 7.2 Hz, 1H, H-6), 7.19 (d, $J_{3,4}$ = 8.7 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 177.5 (C=S), 170.2 (C-2), 144.2 (HC=N), 133.2 (C-10), 132.6 (CH-4), 130.0 (C-9), 128.4 (CH-5), 127.2 (CH-7), 124.3 (CH-6), 120.4 (CH-3), 118.9 (CH-8), 107.7 (C-1); EI-MS m/z (% rel. abund.): 245 (M^+, 35), 169 (100), 141 (18), 128 (12), 115 (25); HREI-MS Calcd for $C_{12}H_{11}N_3OS$: m/z = 245.0623, found 245.0616; Anal. Calcd for $C_{12}H_{11}N_3OS$: C = 58.76; H = 4.52; N = 17.13; Found: C = 58.74; H = 4.55; N = 17.15.

(*E*)-2-(Biphenyl-4-ylmethylene) hydrazinecarbothioamide (28) [39]

Solid; Off white; Yield: 68%; M.P.: 205–207 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.45 (s, 1H, NH), 8.07 (s, 1H, NH), 8.03 (s, 1H, H–C=N), 7.98 (d, $J_{2,3}$ = $J_{6,5}$ = 8.4 Hz, 2H, H-2, H-6), 7.72 (m, 4H, H-3, H-5, H-2′, H-6′), 7.49 (t, $J_{3'(2',4')}$ = $J_{5'(4',6')}$ = 7.2 Hz, 2H, H-3′, H-5′), 7.39 (t, $J_{4'(3',5')}$ = 7.2 Hz, 1H, H-4′); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 177.9 (C=S), 146.2 (HC=N), 142.9 (C-4), 140.7 (C-7), 133.0 (C-1), 129.8 (CH-2), 129.8 (CH-6), 129.0 (CH-9), 129.0 (CH-11), 127.7 (CH-3), 127.7 (CH-5), 127.6 (CH-8), 127.6 (CH-12), 127.3 (CH-10); EI-MS m/z (% rel. abund.): 255 (M^+, 76), 238 (27), 221 (30), 179 (100), 152 (39); HREI-MS Calcd for $C_{14}H_{13}N_3S$: m/z = 255.0830, found 255.0822; Anal. Calcd for $C_{14}H_{13}N_3S$: C = 65.86; H = 5.13; N = 16.46; Found: C = 65.88; H = 5.15; N = 16.49.

(*E*)-2-(4-(Benzyloxy) benzylidene) hydrazinecarbothioamide (35) [40]

Solid; Off white; Yield: 72%; M.P.: 188–190 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.29 (s, 1H, NH), 8.04 (s, 1H, H–C=N), 7.97 (s, 1H, H–NH), 7.89 (bd s, 1H, NH), 7.73 (d, $J_{2,3}$ = $J_{6,5}$ = 8.7 Hz, 2H, H-2, H-6), 7.45 (t,

$J_{9(8,10)} = J_{10(9,11)} = J_{11(10,12)} = 6.9$ Hz, 3H, H-9, H-10, H-11), 7.38 (overlapping multiplet, 2H, H-8, H-12), 7.04 (d, $J_{3,2} = J_{5,6} = 8.7$ Hz, 2H, H-3, H-5), 5.14 (s, 2H, H-CH_2); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 177.8 (C=S), 160.2 (C-4), 146.3 (HC=N), 136.4 (C-7), 130.2 (CH-2), 130.2 (CH-6), 128.7 (CH-9), 128.7 (CH-11), 127.5 (CH-10), 127.0 (CH-8), 127.0 (CH-12), 126.2 (C-1), 114.5 (CH-3), 114.5 (CH-5), 70.6 (CH_2); EI-MS m/z (% rel. abund.): 285 (M^+, 51), 268 (27), 135 (9), 91 (100), 75 (6), 65 (20); HREI-MS Calcd for $C_{15}H_{15}N_3OS$: $m/z = 285.0936$, found 285.0930; Anal. Calcd for $C_{15}H_{15}N_3OS$: C = 63.13; H = 5.30; N = 14.73; Found: C = 63.15; H = 5.32; N = 14.76.

General procedure for the synthesis of (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazole derivatives (2, 3, 5–11, 13–19, 21–27, 29–34, 36–38)

Thiosemicarbazone intermediates (0.5 mmol), different substituted phenacyl bromides (0.5 mmol), and triethyl amine (0.5 mmol) were taken in ethanol into a 100-mL round-bottomed flask and refluxed for 3 h with constant stirring. Progress of the reaction was monitored by the thin-layer chromatography (TLC). After completion, the resulting precipitate was filtered and washed with 5 mL cold ethanol to afford the pure products. Compounds **2**, **3**, **5**–**11**, **13**–**19**, **21**–**27**, **29**–**34**, **36**–**38** were characterized by spectroscopic analysis. To the best of our knowledge, compounds **2**, **3**, **11**, **14**, **16**–**19**, **23**, **27**, and **29**–**34** are new compounds while other compounds are structurally known [41,42].

(*E*)-2-(2-(2,6-Dimethoxybenzylidene)hydrazinyl)-4-(4-methoxyphenyl)thiazole (2)

Solid; Orange; Yield: 78%; M.P.: 145–147 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.80 (s, 1H, NH), 8.21 (s, 1H, H–C=N), 7.77 (d, $J_{2'',3''} = J_{6'',5''} = 8.8$ Hz, 2H, H-2″, H-6″), 7.31 (t, $J_{4(3,5)} = 8.4$ Hz, 1H, H-3), 7.06 (s, 1H, H-5′), 6.95 (d, $J_{3'',2''} = J_{5'',6''} = 8.8$ Hz, 2H, H-3″, H-5″), 6.71 (d, $J_{3,4} = J_{5,4} = 8.4$ Hz, 2H, H-3, H-5), 3.81 (s, 6H, 2H, OCH_3), 3.77 (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.4 (N=C–S), 158.6 (C-4″), 158.3 (C-2), 158.3 (C-6), 147.3 (C-4′), 136.1 (HC=N), 130.3 (CH-4), 126.7 (CH-2″), 126.7 (CH-6″), 123.7 (C-1″), 113.8 (CH-3″), 113.8 (CH-5″), 110.0 (C-1), 104.5 (CH-3), 104.5 (CH-5), 101.2 (CH-5′), 56.0 (OCH_3), 56.0 (OCH_3), 55.0 (OCH_3); EI-MS m/z (% rel. abund.): 369 (M^+, 64), 219 (15), 206 (100), 191 (24), 164 (34), 149 (22); HREI-MS Calcd for $C_{19}H_{19}N_3O_3S$: $m/z = 369.1147$, found 369.1133; Anal. Calcd for $C_{19}H_{19}N_3O_3S$: C = 61.77; H = 5.18; N = 11.37; Found: C = 61.75; H = 5.17; N = 11.35.

(*E*)-2-(2-(2,6-Dimethoxybenzylidene) hydrazinyl)-4-(3-nitrophenyl)thiazole (3)

Solid; Yellow; Yield: 75%; M.P.: 178–180 °C; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.98 (s, 1H, NH), 8.65 (s, 1H, H–C=N), 8.29 (d, $J_{4'',5''} = 7.6$ Hz, 1H, H-4″), 8.24 (s, 1H, H-2″), 8.14 (dd, $J_{6'',4''} = 1.6$ Hz, $J_{6'',5''} = 8.0$ Hz, 1H, H-6″), 7.71 (t, $J_{5''(4'',6'')} = 8.0$ Hz, 1H, H-6″), 7.58 (s, 1H, H-5′), 7.32 (t, $J_{4(3,5)} = 8.4$ Hz, 1H, H-4), 6.72 (d, $J_{3,4} = J_{5,4} = 8.4$ Hz), 3.82 (s, 6H, 2OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 170.6 (N=C–S), 158.4 (C-2), 158.4 (C-6), 148.1 (C-4′), 147.2 (C-3″), 136.7 (HC=N), 131.8 (C-1″), 131.5 (CH-6″), 130.5 (CH-4), 130.1 (CH-2″), 122.8 (CH-4″), 119.8 (CH-5″), 110.1 (C-1), 106.2 (CH-5′), 104.5 (CH-3), 104.5 (CH-5), 56.0 (OCH_3), 56.0 (OCH_3); EI-MS m/z (% rel. abund.): 384 (M^+, 31), 221 (26), 175 (56), 149 (23), 121 (11), 89 (10); HREI-MS Calcd for $C_{18}H_{16}N_4O_4S$: $m/z = 384.0892$, found 384.0967; Anal. Calcd for $C_{18}H_{16}N_4O_4S$: C = 56.24; H = 4.20; N = 14.58; Found: C = 56.27; H = 4.23; N = 14.60.

(*E*)-2-(2-(Naphthalen-1-ylmethylene) hydrazinyl)-4-phenylthiazole (5) [CAS # 464200-44-0]

Solid; Brick brown; Yield: 58%; M.P.: 183–185 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.29 (s, 1H, NH), 8.76 (d, $J_{2,3} = 8.4$ Hz, 1H, H-2), 8.66 (s, 1H, H–C=N), 8.01 (d, $J_{4,3} = 7.8$ Hz, 1H, H-4), 7.98 (d, $J_{5,6} = 7.8$ Hz, 1H, H-5), 7.88 (d, $J_{2'',6''} = J_{6'',5''} = 7.2$ Hz, 2H, H-2″, H-6″), 7.85 (d, $J_{8,7} = 7.2$ Hz, 1H, H-8), 7.68 (t, $J_{7(6,8)} = 7.8$ Hz, 1H, H-7), 7.60 (overlapping multiplet, 2H, H-3, H-6), 7.42 (t, $J_{3''(2,4)} = J_{5''(4'',6'')} = 7.8$ Hz, 2H, H-3″, H-5″), 7.37 (s, 1H, H-5′), 7.31 (t, $J_{4''(3'',5'')} = 7.2$ Hz, 1H, H-4″); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.2 (N=C-S), 150.1 (C-4′), 141.4 (HC=N), 133.2 (C-10), 133.1 (C-1″), 130.5 (CH-4), 130.3 (C-9), 129.0 (CH-5), 129.0 (C-1), 128.6 (CH-3), 128.5 (CH-6), 128.2 (CH-7), 127.5 (CH-2), 127.3 (CH-3″), 127.3 (CH-5″), 126.2 (CH-4″), 125.5 (CH-2″), 125.5 (CH-6″), 123.2 (CH-8), 105.6 (CH-5′); EI-MS m/z (% rel. abund.): 329 (M^+, 68.2), 176 (100), 153 (36), 134 (48), 127 (18); HREI-MS Calcd for $C_{20}H_{15}N_3S$: $m/z = 329.0987$, found 329.0965; Anal. Calcd for $C_{20}H_{15}N_3S$: C = 72.92; H = 4.59; N = 12.76; Found: C = 72.94; H = 4.61; N = 12.78.

(*E*)-2-(2-(Naphthalen-1-ylmethylene) hydrazinyl)-4-*p*-tolylthiazole (6) [41]

Solid; Light brown; Yield: 50%; M.P.: 209–211 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.26 (s, 1H, NH), 8.76 (d, $J_{2,3} = 8.4$ Hz, 1H, H-2), 8.65 (s, 1H, H–C=N), 8.01 (d, $J_{4,3} = 7.8$ Hz, 1H, H-4), 7.97 (d, $J_{5,6} = 7.8$ Hz, 1H, H-5), 7.85 (d, $J_{8,7} = 7.5$ Hz, 1H, H-8), 7.76 (d, $J_{2'',3''} = J_{6'',5''} = 7.8$ Hz, 2H, H-2″, H-6″), 7.68 (t, $J_{7(6,8)} = 7.8$ Hz,

1H, H-7), 7.60 (overlapping multiplet, 2H, H-3, H-6), 7.28 (s, 1H, H-5′), 7.22 (d, $J_{3'',2''} = J_{5'',6''} = 7.8$ Hz, 2H, H-3″, H-5″), 2.32 (s, 3H, H-CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.0 (N=C–S), 150.8 (C-4′), 141.1 (HC=N), 136.8 (C-4″), 133.6 (C-10), 132.0 (C-1″), 129.8 (CH-4), 129.5 (C-9), 129.2 (CH-3″), 129.2 (CH-5″), 128.9 (CH-5), 127.2 (C-1), 127.0 (CH-3), 126.2 (CH-6), 126.1 (CH-7), 125.6 (CH-2), 125.5 (CH-2″), 125.5 (CH-6″), 124.0 (CH-8), 102.8 (CH-5′), 20.8 (CH_3); EI-MS m/z (% rel. abund.): 343 (M^+, 97), 189 (100), 148 (39), 127 (17); HREI-MS Calcd for $C_{21}H_{17}N_3S$: $m/z = 343.1143$, found 343.1124; Anal. Calcd for $C_{21}H_{17}N_3S$: C = 73.44; H = 4.99; N = 12.24; Found: C = 73.47; H = 4.98; N = 12.26.

(*E*)-4-(4-Methoxyphenyl)-2-(2-(naphthalen-1-ylmethylene)hydrazinyl)thiazole (7) [41]

Solid; Dark orange; Yield: 55%; M.P.: 207–209 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.26 (s, 1H, NH), 8.76 (d, $J_{2,3} =$ 8.4 Hz, 1H, H-2), 8.65 (s, 1H, H–C=N), 8.01 (d, $J_{4,3} =$ 8.4 Hz, 1H, H-4), 7.97 (d, $J_{5,6} = 7.8$ Hz, 1H, H-5), 7.85 (d, $J_{8,7} = 7.2$ Hz, 1H, H-8), 7.80 (d, $J_{2'',3''} = 8.4$ Hz, 1H, H-2″), 7.68 (t, $J_{7(6,8)} = 8.4$ Hz, 1H, H-7), 7.60 (overlapping multiplet, 2H, H-3, H-6), 7.18 (s, 1H, H-5′), 6.97 (d, $J_{3'',2''} = J_{5'',6''} = 8.4$ Hz, 2H, H-3″, H-5″), 3.78 (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.7 (N=C–S), 159.4 (C-4″), 150.5 (C-4′), 141.7(HC=N), 133.2 (C-10), 130.7 (CH-4), 130.5 (C-9), 128.8 (CH-5), 128.4 (C-1), 128.3 (CH-2″), 128.3 (CH-6″), 127.6 (CH-3), 126.4 (CH-6), 125.6 (CH-7), 125.5(C-1″), 125.5 (CH-2), 123.4 (CH-8), 114.7 (CH-3″), 114.7 (CH-5″), 105.7 (CH-5′), 55.6 (OCH_3); EI-MS m/z (% rel. abund.): 359 (M^+, 84), 205 (100), 190 (23), 163 (34), 148 (17), 127 (13); HREI-MS Calcd for $C_{21}H_{17}N_3OS$: $m/z = 359.1092$, found 359.1074; Anal. Calcd for $C_{21}H_{17}N_3OS$: C = 70.17; H = 4.77; N = 11.69; Found: C = 70.19; H = 4.75; N = 11.71.

(*E*)-4-(Biphenyl-4-yl)-2-(2-(naphthalen-1-ylmethylene)hydrazinyl)thiazole (8) [CAS # 468750-89-2]

Solid; Orange; Yield: 52%; M.P.: 177–179 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.27 (s, 1H, NH), 8.76 (d, $J_{2,3} = 8.4$ Hz, 1H, H-2), 8.66 (s, 1H, H–C=N), 8.00 (overlapping multiplet, 4H, H-4, H-5, H-2‴, H-6‴), 7.85 (d, $J_{8,7} = 7.2$ Hz, 1H, H-8), 7.72 (overlapping multiplet, 4H, H-2″, H-3″, H-5″, H-6″), 7.66 (t, $J_{7(6,8)} = 7.2$ Hz, 1H, H-7), 7.59 (t, $J_{3(2,4)} = J_{5(4,6)} = 7.2$ Hz, 2H, H-3, H-5), 7.48 (t, $J_{3'''(2''',4''')} = J_{5'''(4''',6''')} = 7.6$ Hz, 2H, 3‴, H-5‴), 7.42 (s, 1H, H-5′), 7.37 (t, $J_{4'''(3''',5''')} = 7.2$ Hz, 1H, H-4‴); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.4 (N=C–S), 150.5 (C-4′), 141.6 (HC=N), 140.8 (C-4″), 140.7 (C-7″), 133.2 (C-10), 131.8 (C-1″), 130.5 (CH-4), 130.1 (C-9), 129.1 (CH-9″), 129.1 (CH-11″), 128.5 (CH-5), 128.4 (C-1), 128.1 (CH-2″), 128.1 (CH-6″), 127.8 (CH-8″), 127.8 (CH-12″), 127.6 (CH-10″), 127.1 (CH-3), 127.0 (CH-3″), 127.0 (CH-5″), 126.4 (CH-6), 125.6 (CH-7), 125.6 (CH-2), 123.4 (CH-8), 105.8 (CH-5′); EI-MS m/z (% rel. abund.): 405 (M^+, 95), 251 (100), 210 (56), 154 (16), 127 (11); HREI-MS Calcd for $C_{26}H_{19}N_3S$: $m/z = 405.1300$, found 405.1324; Anal. Calcd for $C_{26}H_{19}N_3S$: C = 77.01; H = 4.72; N = 10.36; Found: C = 77.03; H = 4.70; N = 10.38.

(*E*)-2-(2-(Naphthalen-1-ylmethylene) hydrazinyl)-4-(3-nitrophenyl)thiazole (9) [CAS # 464200-43-9]

Solid; Yellow; Yield: 47%; M.P.: 228–230 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.42 (s, 1H, NH), 8.77 (d, $J_{2,3} =$ 8.4 Hz, 1H, H-2), 8.69 (d, $J_{2'',6''} = 1.8$ Hz, 1H, H-2″), 8.67 (s, 1H, H–C=N), 8.33 (d, $J_{6'',5''} = 7.8$ Hz, 1H, H-6″), 8.16 (dd, $J_{4'',2''} = 1.8$ Hz, $J_{4'',3''} = 8.4$ Hz, 1H, H-4″), 8.01 (d, $J_{4,3} = 7.8$ Hz, 1H, H-4), 7.99 (d, $J_{5,6} = 8.4$ Hz, 1H, H-5), 7.87 (d, $J_{8,7} = 7.2$ Hz, 1H, H-8), 7.73 (t, $J_{5''(4'',6'')} = 7.8$ Hz, 1H, H-5″), 7.70 (s, 1H, H-5′), 7.69 (t, $J_{7(6,8)} = 7.2$ Hz, 1H, H-7), 7.61 (overlapping multiplet, 2H, H-3, H-6); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 169.8 (N=C–S), 151.3 (C-4′), 148.5 (C-3″), 142.3 (HC=N), 133.8 (C-1″), 133.7 (CH-6″), 133.4 (C-10), 130.8 (CH-2″), 130.7 (CH-4), 130.4 (C-9), 128.9 (CH-5), 128.5 (C-1), 127.9 (CH-3), 126.5 (CH-6), 125.7 (CH-7), 125.7 (CH-2), 123.7 (CH-8), 123.5 (CH-4″), 122.6 (CH-5″), 106.6 (CH-5′); EI-MS m/z (% rel. abund.): 374 (M^+, 34), 220 (100), 175 (30), 154 (15), 127(19); HREI-MS Calcd for $C_{20}H_{14}N_4O_2S$: $m/z = 374.0837$, found 374.0832; Anal. Calcd for $C_{20}H_{14}N_4O_2S$: C = 64.16; H = 3.77; N = 14.96; Found: C = 64.19; H = 3.78; N = 14.94.

(*E*)-4-(4-Bromophenyl)-2-(2-(naphthalen-1-ylmethylene)hydrazinyl)thiazole (10) [CAS # 464211-54-9]

Solid; Pale yellow; Yield: 60%; M.P.: 192–194 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.30 (s, 1H, NH), 8.75 (d, $J_{2,3} =$ 8.4 Hz, 1H, H-2), 8.66 (s, 1H, H–C=N), 8.01 (d, $J_{4,3} =$ 7.8 Hz, 1H, H-4), 7.98 (d, $J_{5,6} = 7.8$ Hz, 1H, H-5), 7.85 (d, $J_{8,7} = 7.2$ Hz, 1H, H-8), 7.83 (d, $J_{2'',3''} = J_{6'',5''} = 8.4$ Hz, 2H, H-2″, $H6''$), 7.68 (t, $J_{7(8,6)} = 7.2$ Hz, 1H, H-7), 7.61 (overlapping multiplet, 4H, H-3, H-6, H-3″, H-5″), 7.45 (s, 1H, H-5′), 3.78 (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.1 (N=C–S), 150.3 (C-4′), 141.5 (HC=N), 133.0 (C-10), 132.1 (CH-3″), 132.1 (CH-5″), 132.0 (C-1″), 130.5 (CH-4), 130.2 (C-9), 128.5 (CH-5), 128.5 (C-1), 128.4 (CH-2″), 128.4 (CH-6″), 127.6 (CH-3), 126.5 (CH-6), 125.6 (CH-7), 125.6 (CH-2), 123.4 (CH-8), 123.3 (C-4″), 105.7 (CH-5′); EI-MS m/z (% rel. abund.): 407 (M^+, 39), 409 (M+2, 36), 256 (100), 214 (15), 174 (22), 154 (16), 127

(20); HREI-MS Calcd for $C_{20}H_{14}BrN_3S$: m/z = 407.0092, found 407.0083; Anal. Calcd for $C_{20}H_{14}BrN_3S$: C = 58.83; H = 3.46; N = 10.29; Found: C = 58.85; H = 3.48; N = 10.31.

(*E*)-4-(3,4-Dichlorophenyl)-2 -(2-(naphthalen-1-ylmethylene) hydrazinyl) thiazole (11)

Solid; Brick red; Yield: 48%; M.P.: 160–162 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.33 (s, 1H, NH), 8.75 (d, $J_{2,3}$ = 8.4 Hz, 1H, H-2), 8.66 (s, 1H, H–C=N), 8.10 (d, $J_{2'',6''}$ = 1.8 Hz, 1H, H-2″), 8.01 (d, $J_{4,3}$ = 7.8 Hz, 1H, H-4), 7.99 (d, $J_{5,6}$ = 8.4 Hz, 1H, H-5), 7.86 (overlapping multiplet, 2H, H-8, H-6″), 7.68 (overlapping multiplet, 2H, H-7, H-5″), 7.61 (m, 3H, H-3, H-6, H-5′); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 168.3 (N=C–S), 150.4 (C-4′), 141.6 (HC=N), 133.6 (C-4″), 133.1 (C-10), 132.7 (C-3″), 132.5 (C-1″), 130.6 (CH-4), 130.5 (CH-5″), 130.2 (C-9), 128.6 (CH-2″), 128.4 (CH-5), 128.3 (C-1), 127.7 (CH-3), 127.3 (CH-6″), 126.3 (CH-6), 125.5 (CH-7), 125.5 (CH-2), 123.3 (CH-8), 105.9 (CH-5′); EI-MS m/z (% rel. abund.): 397 (M^+, 24), 399 (M+2, 18), 401 (M+4, 7), 244 (100), 202 (17), 154 (15), 127 (18); HREI-MS Calcd for $C_{20}H_{13}Cl_2N_3S$: m/z = 397.0207, found 397.0190; Anal. Calcd for $C_{20}H_{13}Cl_2N_3S$: C = 60.31; H = 3.29; N = 10.55; Found: C = 60.33; H = 3.27; N = 10.52.

(*E*)-2-(2-(Naphthalen-2-ylmethylene) hydrazinyl)-4-phenylthiazole (13) [CAS # 1860007-95-9]

Solid; Yellow; Yield: 75%; M.P.: 229–231 °C; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.28 (s, 1H, NH), 8.18 (s, 1H, H-1), 8.04 (s, 1H, H–C=N), 7.96 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.86 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 7.5 Hz, 2H, H-2″, H-6″), 7.54 (dd, $J_{6,8}$ = $J_{7,5}$ = 1.5 Hz, $J_{6,5}$ = $J_{7,8}$ = 9.0 Hz, 2H, H-6, H-7), 7.42 (t, $J_{3''(2'',4'')}$ = $J_{5''(4'',6'')}$ = 7.5 Hz, 2H, H-3″, H-5″), 7.35 (s, 1H, H-5′), 7.31 (t, $J_{4''(3'',5'')}$ = 7.5 Hz, 1H, H-4″); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 150.4 (C-4′), 143.3 (HC=N), 135.9 (C-10), 132.4 (C-9), 132.2 (C-1″), 129.4 (CH-3″), 129.4 (CH-5″), 129.0 (C-2), 128.4 (CH-4″), 128.2 (CH-4), 127.8 (CH-1), 127.6 (CH-8), 127.4 (CH-5), 127.2 (CH-3), 126.3 (CH-2″), 126.3 (CH-6″), 126.1 (CH-6), 126.0 (CH-7), 105.3 (CH-5′); EI-MS m/z (% rel. abund.): 329 (M^+, 56), 176 (100), 154 (9), 134 (34), 127 (13); HREI-MS Calcd for $C_{20}H_{15}N_3S$: m/z = 329.0987, found 329.0969; Anal. Calcd for $C_{20}H_{15}N_3S$: C = 72.92; H = 4.59; N = 12.76; Found: C = 72.94; H = 4.61; N = 12.78.

(*E*)-2-(2-(Naphthalen-2-ylmethylene) hydrazinyl)-4-*p*-tolylthiazole (14)

Solid; Yellow; Yield: 62%; M.P.: 240–242 °C; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.24 (s, 1H, H-NH), 8.18 (s, 1H, H-1), 8.03 (s, 1H, H–C=N), 7.96 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.75 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 4.8 Hz, 2H, H-2″, H-6″), 7.54 (dd, $J_{6,8}$ = $J_{7,5}$ = 2.4 Hz, $J_{6,5}$ = $J_{7,8}$ = 4.5 Hz, 2H, H-6, H-7), 7.27 (s, 1H, H-5′), 7.21 (d, $J_{3'',2''}$ = $J_{5'',6''}$ = 5.1 Hz, 2H, H-3″, H-5″), 2.31 (s, 3H, CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.3 (N=C–S), 150.0 (C-4′), 143.1 (HC=N), 135.6 (C-10), 132.4 (C-9), 130.0 (C-4″), 129.1 (CH-3″), 129.1 (CH-5″), 128.5 (C-1″), 128.1 (C-2), 127.9 (CH-4), 127.4 (CH-2″), 127.4 (CH-6″), 127.3 (CH-1), 126.1 (CH-8), 127.1 (CH-5), 127.0 (CH-3), 126.4 (CH-6), 125.9 (CH-7), 104.7 (CH-5′), 21.1 (CH_3); EI-MS m/z (% rel. abund.): 343 (M^+, 64), 190 (100), 153 (10), 148 (33), 127 (14); HREI-MS Calcd for $C_{21}H_{17}N_3S$: m/z = 343.1143, found 343.1157; Anal. Calcd for $C_{21}H_{17}N_3S$: C = 73.44; H = 4.99; N = 12.24; Found: C = 73.42; H = 4.97; N = 12.26.

(*E*)-4-(4-Methoxyphenyl)-2-(2-(naphthalen-2-ylmethylene) hydrazinyl)thiazole (15) [CAS # 1808939-62-9]

Solid; Dark yellow; Yield: 65%; M.P.: 238–240 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.21 (s, 1H, NH), 8.17 (s, 1H, H-1), 8.03 (s, 1H, H–C=N), 7.96 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.80 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 8.7 Hz, 2H, H-2″, H-6″), 7.55 (overlapping multiplet, 2H, H-6, H-7), 7.17 (s, 1H, H-5′), 6.97 (d, $J_{3'',2''}$ = $J_{5'',6''}$ = 8.7 Hz, 2H, H-3″, H-5″), 3.77 (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.2 (N=C–S), 159.4 (C-4″), 149.8 (C-4′), 143.0 (HC=N), 135.8 (C-10), 132.3 (C-9), 129.0 (C-2), 128.4 (CH-4), 128.3 (CH-2″), 128.3 (CH-6″), 128.2 (CH-1), 127.7 (CH-8), 127.6 (CH-5), 127.4 (CH-3), 126.3 (CH-6), 126.1 (CH-7), 125.4 (C-1″), 114.6 (CH-3″), 114.6 (CH-5″), 104.5 (CH-5′), 55.5 (OCH_3); EI-MS m/z (% rel. abund.): 359 (M^+, 83), 206 (100), 191 (16), 164 (32), 149 (14), 127 (16); HREI-MS Calcd for $C_{21}H_{17}N_3OS$: m/z = 359.1092, found 359.1082; Anal. Calcd for $C_{21}H_{17}N_3OS$: C = 70.17; H = 4.77; N = 11.69; Found: C = 70.19; H = 4.75; N = 11.67.

(*E*)-4-(Biphenyl-4-yl)-2-(2-(naphthalen-2-ylmethylene)hydrazinyl)thiazole (16)

Solid; Yellow; Yield: 66%; M.P.: 279–281 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.28 (s, 1H, NH), 8.20 (s, 1H, H-1), 8.04 (s, 1H, H–C=N), 7.97 (overlapping multiplet, 6H, H-3, H-4, H-5, H-8, H-2″, H-6″), 7.73 (overlapping multiplet, 4H, H-3″, H-5″, H-8″, H-12″), 7.55 (m, 2H, H-6, H-7), 7.49 (t,

$J_{9''(8'',10'')} = J_{11''(10'',12'')}$ =7.5 Hz, 2H, H-9″, H-11″), 7.42 (s, 1H, H-5′), 7.38 (t, $J_{10''(9'',11'')}$ = 7.2 Hz, 1H, H-10″); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 150.2 (C-4′), 143.8 (HC=N), 140.8 (C-4″), 140.7 (C-7″), 136.0 (C-10), 132.5 (C-9), 131.4 (C-1″), 129.3 (CH-9″), 129.3 (CH-11″), 129.2 (C-2), 128.5 (CH-4), 128.4 (CH-1), 127.9 (CH-8), 127.8 (C-10″), 127.7 (CH-2″), 127.7 (CH-6″), 127.6 (CH-8″), 127.6 (CH-12″), 127.5 (CH-5), 127.4 (CH-3″), 127.4 (CH-5″), 127.2 (CH-3), 126.5 (CH-6), 126.3 (CH-7), 105.4 (CH-5′); EI-MS m/z (% rel. abund.): 405 (M^+, 44), 252 (100), 210 (28), 180 (4), 153 (9), 127 (9); HREI-MS Calcd for $C_{26}H_{19}N_3S$: m/z = 405.1300, found 405.1311; Anal. Calcd for $C_{26}H_{19}N_3S$: C = 77.01; H = 4.72; N = 10.36; Found: C = 77.04; H = 4.70; N = 10.34.

(*E*)-2-(2-(Naphthalen-2-ylmethylene) hydrazinyl)-4-(3-nitrophenyl)thiazole (17)

Solid; Yellow; Yield: 67%; M.P.: 232–234 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.39 (s, 1H, NH), 8.64 (s, 1H, H-2″), 8.32 (d, $J_{4,3}$ = 7.8 Hz, 1H, H-4″), 8.20 (s, 1H, H-1), 8.16 (dd, $J_{6'',4''}$ = 2.1 Hz, $J_{6'',5''}$ = 8.1 Hz, 1H, H-6″), 8.05 (s, 1H, H–C=N), 7.97 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.73 (overlapping multiplet, 2H, H-5, H-5′), 7.55 (overlapping multiplet, 2H, H-6, H-7); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 172.4 (N=C–S), 150.9 (C-3″), 150.7 (C-4′), 149.1 (C-1″), 144.5 (HC=N), 136.4 (C-10), 134.0 (CH-6″), 133.0 (C-9), 132.1 (CH-2″), 129.6 (C-2), 128.7 (CH-4), 128.6 (CH-1), 128.0 (CH-8), 127.9 (CH-5), 127.7 (CH-3), 126.8 (CH-6), 126.3 (CH-7), 124.2 (CH-4″), 123.2 (CH-5″), 106.0 (CH-5′); EI-MS m/z (% rel. abund.): 374 (M^+, 25), 221 (100), 175 (26), 153 (24), 127 (17); HREI-MS Calcd for $C_{20}H_{14}N_4O_2S$: m/z = 374.0837, found 374.0868; Anal. Calcd for $C_{20}H_{14}N_4O_2S$: C = 64.16; H = 3.77; N = 14.96; Found: C = 64.18; H = 3.75; N = 14.98.

(*E*)-4-(4-Bromophenyl)-2-(2-(naphthalen-2-ylmethylene)hydrazinyl)thiazole (18)

Solid; Brown; Yield: 68%; M.P.: 263–265 °C; ^{1}H-NMR (500 MHz, DMSO-d_6) 12.28 (s, 1H, H-NH), 8.19 (s, 1H, H-1), 8.04 (s, 1H, H–C=N), 7.96 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.82 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 8.5 Hz, 2H, H-2″, H-6″), 7.60 (d, $J_{3'',2''}$ = $J_{5'',6''}$ = 8.5 Hz, 2H, H-3″, H-5″), 7.54 (m, 2H, H-7, H-8), 7.43 (s, 1H, H-5′); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.3 (N=C–S), 149.9 (C-4′), 143.1 (HC=N), 135.8 (C-10), 132.4 (C-9), 132.2 (CH-3″), 132.2 (CH-5″), 132.1 (C-1″), 129.2 (C-2), 128.5 (CH-4), 128.4 (CH-2″), 128.4 (CH-6″), 128.3 (CH-1), 127.8 (CH-8), 127.7 (CH-5), 127.5 (CH-3), 126.4 (CH-6), 126.2 (CH-7), 123.4 (C-4″), 104.6 (CH-5′); EI-MS m/z (% rel. abund.): 407 (M^+, 39), 409 (M+2, 44), 256 (98), 254 (100), 214 (16), 21 (16), 174 (36), 153 (18), 127 (25); HREI-MS Calcd for $C_{20}H_{14}BrN3S$: m/z = 407.0092, found 407.0088; Anal. Calcd for $C_{20}H_{14}BrN_3S$: C = 58.83; H = 3.46; N = 10.29; Found: C = 58.85; H = 3.49; N = 10.31.

(*E*)-4-(3,4-Dichlorophenyl)-2-(2-(naphthalen-2-ylmethylene) hydrazinyl)thiazole (19)

Solid; Off white; Yield: 58%; M.P.: 235–237 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.29 (s, 1H, NH), 8.19 (s, 1H, H-1), 8.09 (d, $J_{2'',6''}$ = 1.8 Hz, 1H, H-2″), 8.05 (s, 1H, H–C=N), 7.96 (overlapping multiplet, 4H, H-3, H-4, H-5, H-8), 7.86 (dd, $J_{6'',2''}$ = 2.1 Hz, $J_{6'',5''}$ = 8.4 Hz, 1H, H-6″), 7.68 (d, $J_{5'',6''}$ = 8.4 Hz, 1H, H-5″), 7.58 (s, 1H, H-5′), 7.55 (dd, $J_{6,8}$ = $J_{7,5}$ = 2.4 Hz, $J_{6,5}$ = $J_{7,8}$ = 4.5 Hz, 2H, H-6, H-7); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 150.0 (C-4′), 143.3 (HC=N), 136.0 (C-10), 133.3 (C-4″), 133.0 (C-3″), 132.8 (C-1″), 132.6 (C-9), 131.2 (CH-5″), 129.3 (C-2), 129.1 (CH-4), 128.5 (CH-2″), 128.3 (CH-1), 127.9 (CH-8), 127.7 (CH-5), 127.5 (CH-3), 127.2 (CH-6″), 126.5 (CH-6), 126.3 (CH-7), 105.2 (CH-5′); EI-MS m/z (% rel. abund.): 397 (M^+, 49), 399 (M + 2, 33), 246 (80), 244 (100), 208 (15), 202 (20), 127 (21); HREI-MS Calcd for $C_{20}H_{13}Cl_2N_3S$: m/z = 397.0207, found 397.0212; Anal. Calcd for $C_{20}H_{13}Cl_2N_3S$: C = 60.31; H = 3.29; N = 10.55; Found: C = 60.34; H = 3.30; N = 10.57.

(*E*)-1-((2-(4-Phenylthiazol-2-yl) hydrazono)methyl)naphthalen-2-ol (21) [42]

Solid; Green; Yield: 55%; M.P.: 248–250 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.01 (s, 1H, NH), 8.96 (s, 1H, H–C=N), 8.70 (d, $J_{4,3}$ = 8.7 Hz, 1H, H-4), 7.87 (overlapping multiplet, 4H, H-2″, H-3″, H-5″, H-6″), 7.60 (t,$J_{4(3,5)}$ = 7.2 Hz, 1H, H-4″), 7.44 (m, 3H, H-5, H-6, H-7), 7.35 (m, 2H, H-5′, H-6), 7.23 (d, $J_{3,4}$ = 9.0 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 170.2 (C-2), 150.4 (C-4′), 143.1 (HC=N), 133.3 (C-10), 132.8 (CH-4), 132.5 (C-1″), 130.2 (C-9), 129.0 (CH-3″), 129.0 (CH-5″), 128.5 (CH-4″), 128.4 (CH-5), 127.4 (CH-7), 127.2 (CH-2″), 127.2 (CH-6″), 124.5 (CH-6), 120.3 (CH-3), 118.7 (CH-8), 107.8 (C-1), 105.3 (CH-5′); EI-MS m/z (% rel. abund.): 345 (M^+, 79), 328 (100), 176 (92), 170 (35), 134 (39), 115 (17); HREI-MS Calcd for $C_{20}H_{15}N_3OS$: m/z = 345.0936, found 345.0917; Anal. Calcd for $C_{20}H_{15}N_3OS$: C = 69.54; H = 4.38; N = 12.17; Found: C = 69.57; H = 4.40; N = 12.19.

(*E*)-1-((2-(4-*p* -Tolylthiazol-2-yl) hydrazono) methyl)naphthalen-2-ol (22) [CAS # 357650-77-2]

Solid; Light green; Yield: 78%; M.P.: 268–270 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.03 (s, 1H, NH), 8.96 (s, 1H, H–

C=N), 8.69 (d, $J_{4,3}$ = 8.4 Hz, 1H, H-4), 7.87 (d, $J_{5,6}$ = $J_{8,7}$ = 8.7 Hz, 2H, H-5, H-8), 7.76 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 8.1 Hz, 2H, H-2″, H-6″), 7.59 (t, $J_{7(6,8)}$ = 7.8 Hz, 1H, H-7), 7.40 (t, $J_{6(5,7)}$ = 7.5 Hz, 1H, H-6), 7.25 (m, 4H, H-3, H-5′, H-3″, H-4″), 2.31 (s, 3H, H-CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.3 (N=C–S), 170.0 (C-2), 150.2 (C-4′), 143.0 (HC=N), 133.5 (C-10), 132.4 (CH-4), 131.4 (C-4″), 130.2 (C-1″), 130.1 (C-9), 129.3 (CH-3″), 129.3 (CH-5″), 128.6 (CH-5), 127.5 (CH-7), 125.4 (CH-2″), 125.4 (CH-6″), 124.3 (CH-6), 120.1 (CH-3), 118.5 (CH-8), 107.7 (C-1), 105.1 (CH-5′), 21.0 (CH_3); EI-MS m/z (% rel. abund.): 359 (M^+, 77), 342 (100), 190 (89), 170 (32), 148 (27), 115 (20); HREI-MS Calcd for $C_{21}H_{17}N_3OS$: m/z = 359.1092, found 359.1081; Anal. Calcd for $C_{21}H_{17}N_3OS$: C = 70.17; H = 4.77; N = 11.69; Found: C = 70.15; H = 4.75; N = 11.70.

(*E*)-1-((2-(4-(4-Methoxyphenyl)thiazol-2-yl)hydrazono)methyl)naphthalen-2-ol (23)

Solid; Yellow; Yield: 87%; M.P.: 235–237 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.05 (s, 1H, NH), 8.97 (s, 1H, OH), 8.97 (s, 1H, H–C=N), 8.67 (d, $J_{4,3}$ = 8.7 Hz, 1H, H-4), 7.87 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 8.7 Hz, 2H, H-2″, H-6″), 7.80 (d, $J_{5,6}$ = $J_{8,7}$ = 8.7 Hz, 2H, H-5, H-8), 7.59 (t, $J_{7(6,8)}$ = 7.5 Hz, 1H, H-7), 7.40 (t, $J_{6(5,7)}$ = 7.5 Hz, 1H, H-6), 7.23 (d, $J_{3,4}$ = 9.0 Hz, 1H, H-3), 7.15 (s, 1H, H-5′), 6.99 (d, $J_{3'',2''}$ = $J_{5'',6''}$ = 8.7 Hz, 2H, H-3″, H-5″), (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.4 (N=C–S), 170.1 (C-2), 158.7 (C-4″), 150.3 (C-4′), 143.0 (HC=N), 133.1 (C-10), 132.4 (CH-4), 130.2 (C-9), 128.4 (CH-5), 128.3 (CH-2″), 128.3 (CH-6″), 127.3 (CH-7), 125.4 (C-1″), 124.4 (CH-6), 120.2 (CH-3), 118.6 (CH-8), 114.6 (CH-3″), 114.6 (CH-5″), 107.7 (C-1), 105.2 (CH-5′), 54.6 (OCH_3); EI-MS m/z (% rel. abund.): 375 (M^+, 57), 358 (85), 206 (100), 191 (37), 170 (44), 149 (30), 115 (19); HREI-MS Calcd for $C_{21}H_{17}N_3O_2S$: m/z = 375.1041, found 375.1028; Anal. Calcd for $C_{21}H_{17}N_3O_2S$: C = 67.18; H = 4.56; N = 11.19; Found: C = 67.20; H = 4.58; N = 11.20.

(*E*)-1-((2-(4-(Biphenyl-4-yl)thiazol-2-yl)hydrazono)methyl)naphthalen-2-ol (24) [CAS # 468751-46-4]

Solid; Brown; Yield: 80%; M.P.: 248–250 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.01 (s, 1H, H-NH), 8.97 (s, 1H, H–C=N), 8.72 (d, $J_{5,6}$ = $J_{8,7}$ = 8.4 Hz, 2H, H-5, H-8), 7.88 (d, $J_{2'',3''}$ = $J_{6'',5''}$ = 8.7 Hz, 2H, H-2″, H-6″), 7.74 (overlapping multiplet, 4H, H-2‴, H-3″, H-5″, H-6‴), 7.60 (t, $J_{7(6,8)}$ = 7.2 Hz, 1H, H-7), 7.50 (t, $J_{3'''(2''',4''')}$ = $J_{5''(4'',6'')}$ = 7.2 Hz, 2H, H-3‴, H-5‴), 7.41 (overlapping multiplet, 3H, H-6, H-5′, H-4‴), 7.24 (d, $J_{3,4}$ = 9.0 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 170.3 (C-2), 150.5 (C-4′), 143.2 (HC=N), 140.8 (C-4″), 140.7 (C-7″), 133.4 (C-10), 132.6 (CH-4), 131.8 (C-1″), 130.3 (C-9), 129.1 (CH-9″), 129.1 (CH-11″), 128.6 (CH-5), 128.2 (CH-2″), 128.2 (CH-6″), 127.8 (CH-8″), 127.8 (CH-12″), 127.4 (CH-4″), 127.0 (CH-3″), 127.0 (CH-5″), 126.9 (CH-7), 124.6 (CH-6), 120.4 (CH-3), 118.8 (CH-8), 107.9 (C-1), 105.4 (CH-5′); EI-MS m/z (% rel. abund.): 421 (M^+, 53), 404 (66), 252 (100), 210 (36), 170 (31), 115 (11); HREI-MS Calcd for $C_{26}H_{19}N_3OS$: m/z = 421.1249, found 421.1233; Anal. Calcd for $C_{26}H_{19}N_3OS$: C = 74.09; H = 4.54; N = 9.97; Found: C = 74.12; H = 4.55; N = 9.99.

(*E*)-1-((2-(4-(3-Nitrophenyl)thiazol-2-yl)hydrazono)methyl)naphthalen-2-ol (25) [CAS # 307533-15-9]

Solid; Yellow; Yield: 85%; M.P.: 210–212 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.32 (s, 1H, NH), 10.88 (s, 1H, OH), 8.94 (s, 1H, H–C=N), 8.78 (d, $J_{4,3}$ = 8.7 Hz, 1H, H-4), 8.69 (d, $J_{2'',6''}$ = 1.8 Hz, 1H, H-2″), 8.33 (d, $J_{4'',5''}$ = 8.1 Hz, 1H, H-4″), 8.17 (dd, $J_{6'',4''}$ = 1.8 Hz, $J_{6'',5''}$ = 7.8 Hz, 1H, H-6″), 7.87 (d, $J_{5,6}$ = $J_{8,7}$ = 8.7 Hz, 2H, H-5, H-8), 7.74 (overlapping multiplet, 2H, H-5′, H-5″), 7.60 (t, $J_{7(6,8)}$ = 8.1 Hz, 1H, H-7), 7.40 (t, $J_{6(5,7)}$ = 7.8 Hz, 1H, H-6), 7.23 (d, $J_{3,4}$ = 8.7 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 172.0 (N=C–S), 170.5 (C-2), 150.9 (C-4′), 148.8 (C-3″), 143.7 (HC=N), 133.8 (C-1″), 133.7 (CH-6″), 133.5 (C-10), 132.7 (CH-4), 130.5 (CH-2″), 130.4 (C-9), 128.8 (CH-5), 127.6 (CH-7), 124.8 (CH-6), 123.6 (CH-4″), 122.6 (CH-5″), 120.5 (CH-3), 118.9 (CH-8), 108.0 (C-1), 106.1 (CH-5′); EI-MS m/z (% rel. abund.): 390 (M^+, 50), 373 (50), 221 (100), 170 (35), 115 (19); HREI-MS Calcd for $C_{20}H_{14}N_4O_3S$: m/z = 390.0787, found 390.0769; Anal. Calcd for $C_{20}H_{14}N_4O_3S$: C = 61.53; H = 3.61; N = 14.35; Found: C = 61.55; H = 3.63; N = 14.37.

(*E*)-1-((2-(4-(4-Bromophenyl)thiazol-2-yl)hydrazono)methyl)naphthalen-2-ol (26) [CAS # 404016-81-5]

Solid; Green; Yield: 78%; M.P.: 248–250 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.23 (s, 1H, NH), 10.92 (s, 1H, OH), 8.95 (s, 1H, H–C=N), 8.73 (d, $J_{4,3}$ = 8.4 Hz, 1H, H-4), 7.87 (overlapping multiplet, 4H, H-2″, H-3″, H-5″, H-6″), 7.62 (overlapping multiplet, 3H, H-5, H-8, H-5′), 7.43 (overlapping multiplet, 2H, H-6, H-7), 7.23 (d, $J_{3,4}$ = 9.0 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.4 (N=C–S), 170.0 (C-2), 150.3 (C-4′), 143.0 (HC=N), 133.2 (C-10), 132.5 (CH-4), 132.1 (C-1″), 132.0 (CH-3″), 132.0 (CH-5″), 130.2 (C-9), 128.5 (CH-5), 128.4 (CH-2″), 128.4 (CH-6″), 127.3 (CH-7), 124.2 (CH-6), 123.5 (C-4″), 120.1 (CH-3), 118.6 (CH-8), 107.7 (C-1), 105.1 (CH-5′); EI-MS m/z (% rel. abund.): 423 (M^+, 63), 425 (M+2, 61), 406 (62), 256 (100), 213 (21), 170 (48), 115 (38); HREI-MS Calcd for $C_{20}H_{14}BrN_3OS$: m/z = 423.0041, found 423.0026; Anal.

Calcd for $C_{20}H_{14}BrN_3OS$: C = 56.61; H = 3.33; N = 9.90; Found: C = 56.59; H = 3.35; N = 9.92.

(*E*)-1-((2-(4-(3,4-Dichlorophenyl)thiazol-2-yl)hydrazono)methyl)naphthalen-2-ol (27)

Solid; Green; Yield: 88%; M.P.: 248–250 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.24 (s, 1H, NH), 10.90 (s, 1H, OH), 8.95 (s, 1H, H–C=N), 8.76 (d, $J_{4,3}$ = 8.7 Hz, 1H, H-4), 8.10 (d, $J_{2'',6''}$ = 1.8 Hz, 1H, H-2″), 7.87 (d, $J_{5,6} = J_{8,7} = J_{6,5}$ = 8.7 Hz, 3H, H-5, H-8, H-6″), 7.69 (d, $J_{5,6}$ = 8.4 Hz, 1H, H-5″), 7.57 (overlapping multiplet, 2H, H7, H-5′), 7.40 (t, $J_{6(5,7)}$ = 7.8 Hz, 1H, H-6), 7.23 (d, $J_{3,4}$ = 9.0 Hz, 1H, H-3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 170.3 (C-2), 150.4 (C-4′), 143.2 (HC=N), 133.3 (C-4″), 133.2 (C-10), 132.6 (C-3″), 132.5 (C-1″), 132.4 (CH-4), 130.7 (CH-5″), 130.4 (C-9), 128.9 (CH-2″), 128.7 (CH-5), 127.5 (CH-6″), 127.1 (CH-7), 124.6 (CH-6), 120.4 (CH-3), 118.8 (CH-8), 107.9 (C-1), 105.4 (CH-5′); EI-MS m/z (% rel. abund.): 411 (M^+, 22), 413 (M+2, 48),415 (M+4, 26) 396 (45), 340 (17), 244 (100), 202 (27), 170 (68), 115 (21); HREI-MS Calcd for $C_{20}H_{13}Cl_2N_3OS$: m/z = 413.0156, found 413.0149; Anal. Calcd for $C_{20}H_{13}Cl_2N_3OS$: C = 57.98; H = 3.16; N = 10.14; Found: C = 57.96; H = 3.15; N = 10.12.

(*E*)-2-(2-(Biphenyl-4-ylmethylene) hydrazinyl)-4-phenylthiazole (29)

Solid; Yellow; Yield: 70%; M.P.: 234–236 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.21 (s, 1H, NH), 8.06 (s, 1H, H–C=N), 7.86 (d, $J_{2'',3''} = J_{6'',5''}$ = 7.5 Hz, 2H, H-2″, H-6″), 7.74 (overlapping multiplet, 6H, H-2, H-3, H-5, H-6, H-2‴, H-6‴), 7.50 (t, $J_{3''(2'',4'')} = J_{5''(4'',6'')}$ = 7.2 Hz, 2H, H-3″, H-5″), 7.42 (t, $J_{3'''(2''',4''')} = J_{5'''(4''',6''')} = J_{4''(3'',2'')}$ = 7.5 Hz, 3H, H-3‴, H-5‴, H-4″), 7.33 (s, 1H, H-5′), 7.31 (t, $J_{4'''(3''',5''')}$ = 7.5 Hz, 1H, H-4‴); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 150.0 (C-4′), 143.4 (HC=N), 142.8 (C-4), 140.6 (C-7), 133.2 (C-1), 132.7 (C-1″), 129.7 (CH-2), 129.7 (CH-6), 129.2 (CH-3″), 129.2 (CH-5″), 129.0 (CH-9), 129.0 (CH-11), 128.5 (C-4″), 127.8 (CH-3), 127.8 (CH-5), 127.5 (CH-8), 127.5 (CH-12), 127.4 (CH-2″), 127.4 (CH-6″), 127.3 (CH-10), 105.2 (CH-5′); EI-MS m/z (% rel. abund.): 355 (M^+, 61), 176 (100), 152 (14), 134 (34); HREI-MS Calcd for $C_{22}H_{17}N_3S$: m/z = 355.1143, found 355.1144; Anal. Calcd for $C_{22}H_{17}N_3S$: C = 74.34; H = 4.82; N = 11.82; Found: C = 74.36; H = 4.81; N = 11.83.

(*E*)-2-(2-(Biphenyl-4-ylmethylene) hydrazinyl)-4-(4-methoxyphenyl)thiazole (30)

Solid; Yellow; Yield: 65%; M.P.: 233–235 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.17 (s, 1H, NH), 8.05 (s, 1H, H–C=N), 7.79 (d, $J_{2'',3''} = J_{6'',5''}$ = 8.7 Hz, 2H, H-2″, H-6″), 7.76 (overlapping multiplet, 6H, H-2, H-3, H-5, H-6, H-7, H-11), 7.50 (t, $J_{8(7,9)} = J_{10(9,11)}$ = 7.2 Hz, 2H, H-8, H-10), 7.15 (s, 1H, H-5′), 6.97 (d, $J_{3'',2''} = J_{5'',6''}$ = 8.7 Hz, 2H, H-3″, H-5″), 3.77 (s, 3H, OCH_3); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.6 (N=C–S), 159.2 (C-4″), 150.2 (C-4′), 143.5 (HC=N), 142.9 (C-4), 140.7 (C-7), 133.3 (C-1), 129.8 (CH-2), 129.8 (CH-6), 129.3 (CH-9), 129.3 (CH-11), 128.3 (CH-2″), 128.3 (CH-6″), 127.8 (CH-3), 127.8 (CH-5), 127.6 (CH-8), 127.6 (CH-12), 127.4 (CH-10), 125.2 (C-1″), 114.7 (CH-3″), 114.7 (CH-5″), 105.3 (CH-5′), 55.6 (OCH_3); EI-MS m/z (% rel. abund.): 385 (M^+, 100), 206 (83), 191 (16), 180 (11), 164 (28); HREI-MS Calcd for $C_{23}H_{19}N_3OS$: m/z = 385.1249, found 385.1251; Anal. Calcd for C23H19N3OS: C = 71.66; H = 4.97; N = 10.90; Found: C = 71.68; H = 4.99; N = 10.92.

(*E*)-4-(Biphenyl-4-yl)-2-(2-(biphenyl-4-ylmethylene)hydrazinyl)thiazole (31)

Solid; Dark green; Yield: 82%; M.P.: 258–260 °C; ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.25 (s, 1H, NH), 8.07 (s, 1H, H–C=N), 7.95 (d, $J_{2'',3''} = J_{6'',5''}$ = 8.4 Hz, 2H, H-2″, H-6″), 7.74 (overlapping multiplet, 4H, H-2, H-3, H-5, H-6), 7.72 (m, 6H, H-3″, H-5″, H-7″, H-8″, H-10″, H-11″), 7.49 (q, 4H, H-7, H-8, H-10, H-11), 7.41 (s, 1H, H-5′), 7.39 (m, 2H, H-9, H-9″); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 150.1 (C-4′), 143.4 (HC=N), 142.8 (C-4), 140.7 (C-7), 140.6 (C-4″), 140.5 (C-7″), 133.3 (C-1), 131.7 (C-1″), 129.6 (CH-2), 129.6 (CH-6), 129.2 (CH-2″), 129.2 (CH-6″), 129.0 (CH-9), 129.0 (CH-11), 127.8 (CH-9″), 127.8 (CH-11″), 127.7 (CH-3), 127.7 (CH-5), 127.7 (CH-3″), 127.7 (CH-5″), 127.6 (CH-8), 127.6 (CH-12), 127.5 (CH-10), 127.3 (CH-10″), 127.0 (CH-8″), 127.0 (CH-12″), 105.3 (CH-5′); EI-MS m/z (% rel. abund.): 431 (M^+, 53), 252 (100), 210 (29), 180 (11), 152 (10); HREI-MS Calcd for $C_{28}H_{21}N_3S$: m/z = 431.1456, found 431.1311; Anal. Calcd for C28H21N3S: C = 77.93; H = 4.91; N = 9.74; Found: C = 77.96; H = 4.93; N = 9.72.

(*E*)-2-(2-(Biphenyl-4-ylmethylene) hydrazinyl)-4-(3-nitrophenyl)thiazole (32)

Solid; Orange; Yield: 63%; M.P.: 230–232 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.34 (s, 1H, NH), 8.67 (s, 1H, H-2″), 8.31 (d, $J_{4'',5''}$ = 7.8 Hz, 1H, H-4″), 8.16 (dd, $J_{6'',4''}$ = 2.1 Hz, $J_{6'',5''}$ = 8.1 Hz, 1H, H-6″), 8.08 (s, 1H, H–C=N), 7.75 (overlapping multiplet, 4H, H-2, H-3, H-5, H-6), 7.73 (overlapping multiplet, 3H, H-7, H-11, H-5″), 7.67 (s, 1H, H-5′), 7.50 (t, $J_{8(7,9)} = J_{10(9,11)}$ = 7.2 Hz, 2H, H-8, H-10), 7.40 (t, $J_{9(8,10)}$ = 7.2 Hz, 1H, H-9); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.7 (N=C–S), 150.4 (C-4′), 148.6 (C-3″), 143.7 (HC=N), 142.9 (C-4), 140.8 (C-7),

133.8 (C-1″), 133.5 (CH-6″), 133.4 (C-1), 130.4 (CH-2″), 129.9 (CH-2), 129.9 (CH-6), 129.3 (CH-9), 129.3 (CH-11), 127.8 (CH-3), 127.8 (CH-5), 127.6 (CH-8), 127.6 (CH-12), 127.5 (CH-10), 123.8 (CH-4″), 122.8 (CH-5″), 105.8 (CH-5′); EI-MS m/z (% rel. abund.): 400 (M^+, 34), 221 (100), 180 (11), 175 (26), 152 (15); HREI-MS Calcd for $C_{22}H_{16}N_4O_2S$: m/z = 400.0994, found 400.1003; Anal. Calcd for C22H16N4O2S: C = 65.99; H = 4.03; N = 13.99; Found: C = 65.97; H = 4.01; N = 13.97.

(*E*)-2-(2-(Biphenyl-4-ylmethylene) hydrazinyl)-4-(4-bromophenyl)thiazole (33)

Solid; Off white; Yield: 58%; M.P.: 250–252 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.20 (s, 1H, NH), 8.06 (s, 1H, H–C=N), 7.82 (d, $J_{2'',3''} = J_{5'',6''}$ = 8.7 Hz, 2H, H-2″, H-6″), 7.74 (overlapping multiplet, 4H, H-2, H-3, H-5, H-6), 7.72 (d, $J_{7,8} = J_{11,10}$ = 7.2 Hz, 2H, H-7, H-11), 7.60 (d, $J_{3'',2''} = J_{5'',6''}$ = 8.7 Hz, 2H, H-3″, H-5″), 7.50 (t, $J_{8(7,9)} = J_{10(9,11)}$ = 7.2 Hz, 2H, H-8, H-10), 7.42 (s, 1H, H-5′), 7.40 (t, $J_{9(8,10)}$ = 7.2 Hz, 1H, H-9); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.4 (N=C–S), 149.9 (C-4′), 143.2 (HC=N), 142.7 (C-4), 140.6 (C-7), 133.0 (C-1), 132.1 (C-1″), 132.0 (CH-3″), 132.0 (CH-5″), 129.6 (CH-2), 129.6 (CH-6), 129.0 (CH-9), 129.0 (CH-11), 128.2 (CH-2″), 128.2 (CH-6″), 127.7 (CH-3), 127.7 (CH-5), 127.5 (CH-8), 127.5 (CH-12), 127.3 (CH-10), 123.3 (C-4″), 105.0 (CH-5′); EI-MS m/z (% rel. abund.): 433 (M^+, 48), 435 (M+2, 53), 256 (100), 214 (11), 174 (25), 152 (16); HREI-MS Calcd for $C_{22}H_{16}BrN_3S$: m/z = 433.0248, found 433.0237; Anal. Calcd for $C_{22}H_{16}BrN_3S$: C = 60.84; H = 3.71; N = 9.67; Found: C = 60.86; H = 3.73; N = 9.66.

(*E*)-2-(2-(Biphenyl-4-ylmethylene) hydrazinyl)-4-(3,4-dichlorophenyl)thiazole (34)

Solid; Light yellow; Yield: 46%; M.P.: 220–222 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.25 (s, 1H, NH), 8.08 (overlapping multiplet, 2H, H-2″, H–C=N), 7.85 (dd, $J_{6'',2''}$ = 1.8 Hz, $J_{6'',5''}$ = 8.4 Hz, 1H, H-6″), 7.74 (overlapping multiplet, 4H, H-2, H-3, H-5, H-6), 7.72 (m, 3H, H-7, H-11, H-5″), 7.56 (s, 1H, H-5′), 7.50 (t, $J_{8(7,9)} = J_{10(9,11)}$ = 7.2 Hz, 2H, H-8, H-10); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.6 (N=C–S), 150.1 (C-4′), 143.3 (HC=N), 142.8 (C-4), 140.7 (C-7), 133.5 (C-4″), 133.2 (C-1), 132.6 (C-3″), 132.8 (C-1″), 130.7 (CH-5″), 129.7 (CH-2), 129.7 (CH-6), 129.1 (CH-9), 129.1 (CH-11), 128.7 (CH-2″), 127.7 (CH-3), 127.7 (CH-5), 127.6 (CH-8), 127.6 (CH-12), 127.4 (CH-10), 127.2 (CH-6″), 105.2 (CH-5′); EI-MS m/z (% rel. abund.): 423 (M^+, 56), 425 (M+2, 35), 243 (100), 202 (18), 180 (14), 152 (16); HREI-MS Calcd for $C_{22}H_{15}Cl_2N_3S$: m/z = 423.0364, found 423.0364; Anal. Calcd for $C_{22}H_{15}Cl_2N_3S$: C = 62.27; H = 3.56; N = 9.90; Found: C = 62.30; H = 3.58; N = 9.92.

(*E*)-2-(2-(4-(Benzyloxy)benzylidene) hydrazinyl)-4-(4-methoxyphenyl)thiazole (36) [CAS # 1808939-63-0]

Solid; Orange; Yield: 62%; M.P.: 204–206 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.96 (s, 1H, NH), 7.95 (s, 1H, H–C=N), 7.78 (d, $J_{2,3} = J_{6,5}$ = 8.7 Hz, 2H, H-2, H-6), 7.59 (d, $J_{2'',3''} = J_{6'',5''}$ = 9.0 Hz, 2H, H-2″, H-6″), 7.46 (t, $J_{9(8,10)} = J_{10(9,11)} = J_{11(10,12)}$ = 9.0 Hz, 3H, H-9, H-10, H-11), 7.39, (overlapping multiplet, 2H, H-8, H-12), 7.11 (s, 1H, H-5′), 7.08 (d, $J_{3,2} = J_{5,6}$ = 8.7 Hz, 2H, H-3, H-5), 6.96 (d, $J_{3'',2''} = J_{5'',6''}$ = 9.0 Hz, 2H, H-3″, H-5″), 5.14 (s, 2H, H-CH_2); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.4 (N=C–S), 160.2 (C-4), 158.7 (C-4″), 149.9 (C-4′), 143.5 (HC=N), 136.4 (C-7), 130.2 (CH-2), 130.2 (CH-6), 128.7 (CH-9), 128.7 (CH-11), 128.3 (CH-2″), 128.3 (CH-6″), 127.5 (CH-10), 127.0 (CH-8), 127.0 (CH-12), 126.2 (C-1), 125.4 (C-1″), 114.6 (CH-3″), 114.6 (CH-5″), 114.5 (CH-3), 114.5 (CH-5), 105.2 (CH-5′), 70.6 (CH_2), 55.5 (OCH_3); EI-MS m/z (% rel. abund.): 415 (M^+, 51), 206 (100), 191 (14), 164 (20), 149 (19), 134 (11), 91 (84); HREI-MS Calcd for $C_{24}H_{21}N_3O_2S$: m/z = 415.1354, found 415.1340; Anal. Calcd for $C_{24}H_{21}N_3O_2S$: C = 69.38; H = 5.09; N = 10.11; Found: C = 69.40; H = 5.11; N = 10.13.

(*E*)-2-(2-(4-(Benzyloxy)benzylidene) hydrazinyl)-4-(biphenyl-4-yl)thiazole (37) [CAS # 468750-68-7]

Solid; Dark brown; Yield: 77%; M.P.: 235–237 °C; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.03 (s, 1H, NH), 7.98 (s, 1H, H–C=N), 7.94 (d, $J_{2'',3''} = J_{6'',5''}$ =8.5 Hz, 2H, H-2″, H-6″), 7.71(d, $J_{2,3} = J_{6,5} = J_{3'',2''} = J_{5'',6''}$ = 8.0 Hz, 4H, H-2, H-6, H-3″, H-5″), 7.60 (d, $J_{8'',9''} = J_{12'',11''}$ = 9.0 Hz, 2H, H-8″, H-12″), 7.48 (overlapping multiplet, 4H, H-8, H-12, H-9″, H-11″), 7.41 (t, $J_{9(8,10)} = J_{11(10,12)}$ = 7.5 Hz, 2H, H-9, H-11), 7.36 (overlapping multiplet, 3H, H-10, H-5′, H-10″), 7.08 (d, $J_{3,2} = J_{5,6}$ = 8.1 Hz, 2H, H-3, H-5), 5.14 (s, 2H, H-CH_2); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.5 (N=C–S), 160.3 (C-4), 150.1 (C-4′), 143.7 (HC=N), 140.7 (C-4″), 140.6 (C-7″), 136.5 (C-7), 130.6 (C-1″), 130.4 (CH-2), 130.4 (CH-6), 129.3 (CH-2″), 129.3 (CH-6″), 128.8 (CH-9), 128.8 (CH-11), 128.4 (CH-9″), 128.4 (CH-11″), 127.8 (CH-3″), 127.8 (CH-5″), 127.7 (CH-10), 127.2 (CH-8″), 127.2 (CH-12″), 127.0 (CH-8), 127.0 (CH-12), 126.9 (CH-10″), 126.3 (C-1), 114.4 (CH-3), 114.4 (CH-5), 105.2 (CH-5′), 70.7 (CH_2); EI-MS m/z (% rel. abund.): 461 (M^+, 59), 252 (100), 238 (11), 210 (26), 165 (8), 91 (79); HREI-MS Calcd for $C_{29}H_{23}N_3OS$: m/z = 461.1562, found 461.1543; Anal.

Calcd for $C_{29}H_{23}N_3OS$: C = 75.46; H = 5.02; N = 9.10; Found: C = 75.49; H = 5.04; N = 9.12.

(*E*)-2-(2-(4-(Benzyloxy)benzylidene) hydrazinyl)-4-(3-nitrophenyl)thiazole (38) [CAS # 469871-00-9]

Solid; Orange; Yield: 58%; M.P.: 207–209 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 12.14 (s, 1H, NH), 8.66 (s, 1H, H-2″), 8.30 (d, $J_{4'',5''}$ = 7.8 Hz, 1H, H-4″), 8.15 (dd, $J_{6'',2''}$ = 2.1 Hz, $J_{6'',5''}$ = 8.1 Hz, 1H, H-6″), 7.98 (s, 1H, H–C=N), 7.72 (t, $J_{5''(4'',6'')}$ = 8.1 Hz, 1H, H-5″), 7.63 (overlapping multiplet, 3H, H-2, H-6, H-5′), 7.47 (t, $J_{9(8,10)} = J_{10(9,11)} = J_{11(10,12)}$ = 8.7 Hz, 3H, H-9, H-10, H-11), 7.39, (overlapping multiplet, 2H, H-8, H-12), 7.08 (d, $J_{3,2} = J_{5,6}$ = 8.7 Hz, 2H, H-3, H-5), 5.14 (s, 2H, H-CH_2); ^{13}C-NMR (125 MHz, DMSO-d_6) : δ 171.8 (N=C–S), 160.3 (C-4), 150.3 (C-4′), 148.9 (C-3″), 143.9 (HC=N), 136.6 (C-7), 133.7 (C-1″), 133.5 (CH-6″), 130.8 (CH-2″), 130.3 (CH-2), 130.3 (CH-6), 128.8 (CH-9), 128.8 (CH-11), 127.7 (CH-10), 127.2 (CH-8), 127.2 (CH-12), 126.3 (C-1), 123.8 (CH-4″), 122.6 (CH-5″), 114.6 (CH-3), 114.6 (CH-5), 105.7 (CH-5′), 70.8 (CH_2); EI-MS m/z (% rel. abund.): 430 (M^+, 15), 221 (81), 191 (11), 175 (9), 91 (100); HREI-MS Calcd for $C_{23}H_{18}N_4O_3S$: m/z = 430.1100, found 430.1109; Anal. Calcd for $C_{23}H_{18}N_4O_3S$: C = 64.17; H = 4.21; N = 13.02; Found: C = 64.20; H = 4.23; N = 13.00.

In vitro α-glucosidase inhibition assay

The α-glucosidase inhibitory profile of all synthesized (*E*)-2-(2-(arylmethylene)hydrazinyl)-4-arylthiazoles and intermediates was measured by following a reported method [43]. Typically, α-glucosidase activity was performed in phosphate buffer 50 mM of pH 6.8 which contains 5% v/v dimethylsulfoxide and PNP glycoside was used as a substrate. The inhibitors were pre-incubated with enzyme for half an hour at 37 °C. Then substrate was added and the enzymatic reaction was performed for 60 s at 37 °C. Absorbance was measured spectrophotometrically at 400 nm. The assay was carried at five different concentrations around the IC_{50} values that were roughly calculated in the first turn of the experiments, and the mean values were adopted.

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