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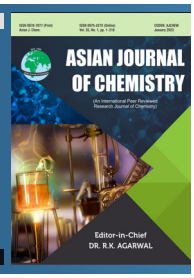

A Facile Synthesis of Thiazole Derivatives bearing Imidazole Moiety, Schiff Bases and their O-Glucosides

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A unique approach for the synthesis of new thiazole O-glycosides is presented in this work. 2-Amino-4-hydroxy-phenyl-1,3-thiazole-5-carboxaldehyde (**3a**) was reacted with phenyl glyoxal and benzil to form 4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazol-2-amine (**4a**) and 4-(4-hydroxy-phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)-thiazol-2-amine (**4b**), respectively. A series of substituted Schiff bases of **4a** and **4b** were synthesized reacting with various aryl aldehyde to form 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazoles (**5a-e**) and 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)-thiazoles (**5f-j**). Glucosylation of compounds (**5a-j**) have been done by using acetobromoglucose as glucosyl donor to afford 2-(imino substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazoles (**6a-e**) and 2-(imino substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)-thiazoles (**6f-j**) further on deacetylation to produce 2-(imino substituted benzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazoles and 2-(imino substituted benzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)-thiazoles (**7f-j**). The synthesized compounds were characterized by elemental analyses, FTIR, ^{1}H & ^{13}C NMR and electron mass spectra (EI-MS) techniques and then screened for their *in vitro* antimicrobial activity.

Keywords: Glucosylation, Imidazole, O-glucosides, Schiff bases, Thiazole.

INTRODUCTION

Penicillin and vitamin B_1 (thiamine) are two examples of natural compounds that have the structural motif of thiazole. Antibacterial, antifungal [1], anti-inflammatory [2], antiviral [3], antimalarial [4] and anti-HIV activities [5] are among the many pharmacological and biological characteristics of thiazole moiety. Analog of thiazole can bind to estrogen receptor ligands [6], neuropeptides [7] and Y5 adenosine receptors [8]. They have been shown to inhibit the human platelet aggregation factor [9], urokinase [10] and poly (ADP-ribose) polymerase-1 [11]. Thiazoles are also used in the production of pain-relieving medicines [12,13] and also work as antithrombotic fibrinogenic receptor antagonists [14], as novel bacterial DNA gyrase B inhibitors [15], *etc*.

Imidazole based compounds have implicit applications such as anticancer, antihypertensive, antihistamine, antipsychotic, hypothermic, cytotoxic, antibacterial, antioxidant *etc.* [16,17]. The highly substituted imidazole shows a high medicinal value for the chemical and biochemical processes [18] and has potential applications such as analgesic, anti-inflammatory [19], fungicidal, antibacterial [20] and anti-tumour activities [21]. O-Glucoside, which has high therapeutic potential, is abundantly dispersed across the plant world, particularly in the roots, seeds, leaves and bark of plants [22,23]. Increasing the solubility of organic molecules in water and lowering the toxicity of aglycone fraction are two of O-glucosides' most significant functions. The Koenigs Knorr method is the most favoured technique for glucosylation of compounds [24]. O-Glucosylation has been synthesized by employing the modified Michael methodology [25]. The operation activity of compounds is mostly associated with the presence of azomethine group (>C=N). These azomethines make up one of the most potent groups of molecules with a wide range of biological uses [26-28]. Therefore, it was advised to synthesize novel compounds having thiazole, imidazole, O-glucoside and azo-

methine moiety in one framework as persistence of our research effort and bearing in mind the numerous and important biological func-tions. In this work, 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles, 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles. Moreover, the antimicrobial and antifungal activity were also evaluated since, the presence of all of the aforementioned heterocyclic rings in the same molecular framework may have a synergistic effect on the synthesized compounds.

EXPERIMENTAL

All the chemicals and solvents were bought from Himedia and Merck. Before usage, all the solvents were distilled. All melting points were measured in an open capillary tube over a liquid paraffin bath and are uncorrected. For TLC, silica gel 60 F_{254} was used (Merck). The Bruker FT-IR spectrometer was used to record the IR spectra. The Brucker AC 400 (MHz) analyzer was used to record the ^{1}H NMR and ^{13}C NMR spectra. The spectra are displayed on a scale in parts per million based on an internal standard (trimethylsilane) on the δ scale. The Perkin-Elmer 2400 CHN analyzer was used to analyze the elemental composition of the synthesized compounds.

Synthesis of 4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazol-2-amine (4a): Compound **4** was synthesized according to the reported method [29]. In brief, a composition of glacial acetic acid (50 mL), phenyl glyoxal (0.662 g, 5 mmol), ammonium acetate (0.77 g, 10 mmol), 2-amino-4-(4-hydroxy-phenyl)-1,3-thiazole-5-carboxaldehyde (5 mmol) and phenyl glyoxal were refluxed for 2 h. It was then added to 200 mL of ice-cold water and neutralized with NH_4OH. The resulting dark solid was filtered, washed with distilled water and recrystallized with absolute ethanol. Yield 78%, m.p.: 283 ºC. IR (KBr, ν_{max}, cm^{-1}): 3505 (OH), 3425-3255 (NH_2 *str.*), 3125 (NH *str.*), 3075 (CH-arom *str.*), 1605 (C=C arom *str.*), 1215 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.25 (H, s, -NH), 7.40-8.30 (9H, m, Ar-H), 7.38 (1H, s, imidazole-H), 7.15 (2H, s, -NH_2), 5.43 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 171.2 (N=C-S), 157.3 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 118-131 (aromatic 12C-atom), 117.9 (NH=C-C), 115.5 (C=C-S) (thiazole). EI-MS: *m/z* (%) 336 (2%), 336 (4%), 335 (22%), 334 (100%) base peak. Anal. calcd. (found) % for $C_{18}H_{14}N_4OS$: C, 64.65 (65.20); H, 4.22 (4.43); N, 16.75 (16.95); S, 9.59 (10.07); O, 4.78 (4.95).

Synthesis of 4-(4-hydroxy phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazol-2-amine (4b): A mixture of 2-amino-4-(4-hydroxyphenyl)-1,3-thiazole-5-carboxaldehyde (5 mmol), benzil (0.662 g, 5 mmol), CH_3COONH_4 (0.77 g, 10 mmol) and glacial acetic acid (50 mL) were refluxed for 2 h. It was then added to 200 mL of ice-cold water and neutralized with NH_4OH. The resulting dark brown solid was filtered, washed with distilled water and recrystallized with absolute ethanol. Yield 75%, m.p.: 265 ºC. IR (KBr, ν_{max}, cm^{-1}): 3515 (OH), 3440-3240 (NH_2 *str.*), 3137 (NH *str.*), 3060 (CH-arom *str.*), 1560 (C=C arom *str.*), 1240 (C-S *str.*). ^{1}H NMR δ_H (DMSO-d_6, 400 MHz): 13.12 (H, s, -NH), 7.39-8.35 (10H, m, Ar-H), 7.37 (1H, s, imidazole-H), 7.27 (2H, s, -NH_2), 5.63 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 172.2 (N=C-S), 158.3 (C=C-N), 143.1 (C=C-N) (imidazole), 131.8 (N=C-NH), 117-131 (arom. 18C-atom), 116.2 (NH=C-C), 115.5 (C=C-S) (thiazole). EI-MS: *m/z* (%) 413 (1%), 412 (3%), 412 (5%), 411 (28%), 410 (100%) base peak. Anal. calcd. (found) % for $C_{24}H_{18}N_4OS$: C, 70.22 (70.65); H, 4.42 (4.49); N, 13.65 (13.95); S, 7.81 (8.07); O, 3.90 (4.05).

Synthesis of 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (5a-e): A solution of 4-phenyl-5-(4-hydroxyphenyl-1*H*-imidazol-2-yl)thiazol-2-amine (0.1 mol) and substituted benzaldehyde (0.1 mol) was dissolved in ethanol using a catalytic amount of glacial acetic acid. The reaction mixture was refluxed with constant stirring at 50-60 ºC for 4-5 h. Then, the progress of the reaction is checked by TLC. It was cooled at room temperature and the product was filtered, dried by ether and recrystallized from hot ethanol. The product was washed with sodium bisulphite to get rid of extra aldehyde and then with cooled ethanol to get pure product.

2-(Iminobenzal)-4-hydroxy-phenyl-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (5a): Yield 75%, m.p.: 140 ºC. IR (KBr, ν_{max}, cm^{-1}): 3525 (OH), 3160 (NH atom *str.*), 3015 (CH-atom *str.*), 1612 (C=C atom *str.*), 1320 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.87 (H, s, NH), 8.88 (H, s, CH), 7.39 (H, s, imidazole-H), 6.90-8.32 (14H, m, Ar-H), 5.54 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 174.4 (N=C-S), 161.2 (CH=N), 160.5 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 121.9 (NH=C-C), 116-154 (arom. 18 C-atom). EI-MS: *m/z* (%) 425 (1%), 424 (4%), 424 (5%), 423 (30%), 422 (100%) base peak. Anal. calcd. (found) % for $C_{25}H_{18}N_4OS$: C, 71.07 (72.58); H, 4.29 (4.55); N, 13.26 (13.72); S, 7.56 (7.89); O, 3.79 (3.99).

2-(Imino-4-chlorobenzal)-4-hydroxy-phenyl-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (5b): Yield 75%, m.p.: 195 ºC. IR (KBr, ν_{max}, cm^{-1}): 3505 (OH), 3165 (NH atom *str.*), 3024 (CH-atom *str.*), 1618 (C=C atom *str.*), 1332 (C-S *str.*), 755 (C-Cl *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.43 (H, s, NH), 8.76 (H, s, CH), 7.46-8.13 (13H, m, Ar-H), 7.45 (H, s, imidazole-H), 5.50 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 173.3 (N=C-S), 161.2 (CH=N), 159.1 (C=C-N), 141.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 130.2 (C=C-S) (thiazole), 127-136 (aromatic 18C-atom), 115.9 (NH=C-C). EI-MS: *m/z* (%) 460 (2%), 460 (1%), 459 (11%), 458 (4%), 458 (37%), 457 (29%), 456 (100%) base peak. Anal. calcd. (found) % for $C_{25}H_{17}N_4OSCl$: C, 65.71 (66.10); H, 3.75 (3.89); Cl, 7.76 (7.93); N, 12.26 (12.67); S, 7.02 (7.27); O, 3.50 (3.76).

2-(Imino-4-nitrobenzal)-4-hydroxyphenyl-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (5c): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3520 (OH), 3156 (NH *str.*), 3015 (CH-atom. *str.*), 1624 (C=C atom *str.*), 1540 asymmetric, 1340 symmetric (NO_2 gp), 1338 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.42 (H, s, Ar-H), 8.72 (H, s, CH), 8.29 (2H, d, Ar-H), 8.21 (H, s, imidazole-H), 6.90-8.32 (13H, m, Ar-H), 5.86 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 171.3 (N=C-S), 162.0 (CH=N), 159.1 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 126.2 (C=C-S) (thiazole), 124-150 (aromatic 18C-atom), 121.9 (NH=C-C). EI-MS: *m/z* (%) 470

(1%), 469 (5%), 469 (4%), 468 (27), 468 (3%), 467 (100%) base peak. Anal. calcd. (found) % for $C_{25}H_{17}O_3N_5S$: C, 64.23 (65.04); H, 3.67 (3.75); O, 10.27 (10.48); N, 14.98 (15.20); S, 6.86 (7.08).

2-(Imino-4-methoxybenzal)-4-hydroxy-phenyl-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (5d): Yield 68%, m.p.: 212 ºC. IR (KBr, ν_{max}, cm^{-1}): 3528 (OH), 3164 (NH *str.*), 3020 (CH-atom *str.*), 1615 (C=C atom *str.*), 1322 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.48 (H, s, NH), 8.64 (H, s, CH), 8.25 (H, s, imidazole-H), 6.90-8.60 (13H, m, Ar-H), 5.55 (1H, s, OH), 3.92 (3H, s, OCH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 170.3 (N=C-S), 161.0 (CH=N), 158.1 (C=C-N), 141.1 (C=C-N) (imidazole), 131.8 (N=C-NH), 125.2 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 121.9 (NH=C-C), 56.32 (-OCH_3). EI-MS: *m/z* (%) 455 (1%), 454 (4%), 454 (6%), 453 (30), 452 (100%) base pea. Anal. calcd. (found) % for $C_{26}H_{20}O_2N_4S$: C, 69.01 (70.04); H, 4.45 (4.75); O, 7.07 (7.48); N, 12.38 (12.60); S, 7.09 (7.50).

2-(Imino-4-methylbenzal)-4-hydroxy-phenyl-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (5e): Yield 75%, m.p.: 227 ºC. IR (KBr, ν_{max}, cm^{-1}): 3510 (OH), 3154 (NH *str.*), 3016 (CH-atom *str.*), 1605 (C=C atom *str.*), 1318 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.88 (H, s, CH), 8.42 (H, s, imidazole-H), 6.90-8.30 (13H, m, Ar-H), 5.45 (1H, s, OH), 2.95 (3H, s, CH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.7 (CH=N), 158.9 (C=C-N), 141.6 (C=C-N) (imidazole), 131.7 (N=C-NH), 125.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 122.4 (NH=C-C), 21.9 (-CH_3). EI-MS: *m/z* (%) 439 (1%), 438 (5%), 438 (4.5%), 437 (29), 437 (1%), 436 (100%) base peak. Anal. calcd. (found) % for $C_{26}H_{20}ON_4S$: C, 71.54 (72.31); H, 4.62 (4.84); O, 3.67 (3.48); N, 12.83 (12.61); S, 7.35 (7.58).

General procedure for the synthesis of 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles (5f-j): To a solution of 4,5-diphenyl-5-(4-hydroxy-phenyl-1*H*-imidazol-2-yl)thiazol-2-amines (0.1 mol) and substituted benzaldehyde (0.1 mol) were dissolved in ethanol using a catalytic amount of glacial acetic acid. The reaction mixture was refluxed with constant stirring at 50-60 ºC for 4-5 h. The progress of the reaction was checked by TLC. It was cooled at room temperature and the product was filtered, dried by ether and recrystallized from hot ethanol. The product was washed with sodium bisulphite to get rid of excess aldehyde followed by ethanol to get pure product.

2-(Iminobenzal)-4-hydroxy-phenyl-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (5f): Yield 65%, m.p.: 231 ºC. IR (KBr, ν_{max}, cm^{-1}): 3520 (OH), 3435 (NH *str.*), 3045 (CH-atom *str.*), 1592 (C=C atom *str.*), 1699 (C=N), 1320 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.57 (H, s, NH), 8.98 (H, s, CH), 6.90-7.83 (19H, m, Ar-H), 5.54 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 174.9 (N=C-S), 161.8 (CH=N), 159.9 (C=C-N), 132.8 (N=C-NH), 130.1 (C=C-N) (imidazole), 128.8 (C=C-S) (thiazole), 121.9 (NH=C-C), 120-138 (aromatic 24C-atom). EI-MS: *m/z* (%) 501 (1%), 500 (5%), 500 (4%), 499 (35%), 498 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{22}N_4OS$: C, 74.68 (74.98); H, 4.45 (4.86); N, 11.24 (12.02); S, 6.43 (6.89); O, 3.21 (3.98).

2-(Imino-4-chlorobenzal)-4-hydroxy-phenyl-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (5g): Yield 78%, m.p.: 198 ºC. IR (KBr, ν_{max}, cm^{-1}): 3505 (OH), 3443 (NH *str.*), 3040 (CH-atom *str.*, 1585 (C=C atom *str.*), 1687 (C=N), 1317 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.42 (H, s, NH), 8.65 (H, s, CH), 6.46-7.58 (18H, m, Ar-H), 5.54 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 174.5 (N=C-S), 160.9 (CH=N), 159.8 (C=C-N), 132.5 (N=C-NH), 130.1 (C=C-N) (imidazole), 129.2 (C=C-S) (thiazole), 117-138 (aromatic 24C-atom). EI-MS: *m/z* (%) 536 (2%), 536 (1%), 535 (13%), 534 (6%), 534 (37%), 533 (34%), 533 (2%), 532 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{21}N_4OSCl$: C, 69.85 (70.10); H, 3.97 (4.09); Cl, 6.65 (6.93); N, 10.51 (10.77); S, 6.02 (6.65); O, 3.00 (3.29).

2-(Imino-4-nitrobenzal)-4-hydroxy-phenyl-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (5h): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3515 (OH), 3447 (NH *str.*), 3050 (CH-atom *str.*), 1595 (C=C atom *str.*), 1675 (C=N), 1332 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.39 (H, s, NH), 8.41 (H, s, Ar-H), 8.72 (H, s, CH), 6.90-8.32 (18H, m, Ar-H), 5.36 (1H, s, OH). ^{13}C NMR (DMSO-d_6), δ ppm: 174.3 (N=C-S), 162.8 (CH=N), 159.8 (C=C-N), 142.1 (C=C-N) (imidazole), 133.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 124-160 (aromatic 24C-atom), 120.9 (NH-C=C). EI-MS: *m/z* (%) 556 (2%), 545 (7%), 545 (4%), 544 (2%), 544 (34%), 543 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{21}O_3N_5S$: C, 68.49 (69.04); H, 3.89 (4.05); O, 8.83 (9.04); N, 12.88 (12.94); S, 5.90 (6.08).

2-(Imino-4-methoxybenzal)-4-hydroxy-phenyl-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (5i): Yield 67%, m.p.: 259 ºC. IR (KBr, ν_{max}, cm^{-1}): 3507 (OH), 3433 (NH *str.*), 3032 (CH-atom *str.*), 1566 (C=C atom *str.*), 1667 (C=N), 1335 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.75 (H, s, NH), 8.85 (H, s, CH), 6.90-7.85 (18H, m, Ar-H), 5.58 (1H, s, OH), 3.98 (3H, s, OCH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 173.9 (N=C-S), 162.5 (CH=N), 135.3 (C=C-N), 135.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 114-165 (aromatic 24C-atom), 121.9 (NH=C-C), 56.3 (-OCH_3). EI-MS: *m/z* (%) 531 (2%), 530 (6%), 530 (5%), 529 (35%), 529 (2%), 528 (100%) base peak. Anal. calcd. (found) % for $C_{32}H_{24}O_2N_4S$: C, 72.71 (73.04); H, 4.58 (4.79); O, 6.05 (6.78); N, 10.60 (11.06); S, 6.07 (7.20).

2-(Imino-4-methylbenzal)-4-hydroxy-phenyl-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (5j): Yield 65%, m.p.: 276 ºC. IR (KBr, ν_{max}, cm^{-1}): 3510 (OH), 3445 (NH *str.*), 3042 (CH-atom *str.*), 1570 (C=C atom *str.*), 1672 (C=N), 1343 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.82 (H, s, NH), 8.76 (H, s, CH), 6.90-7.53 (18H, m, Ar-H), 5.65 (1H, s, OH), 2.75 (3H, s, CH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.9 (CH=N), 159.9 (C=C-N), 142.6 (C=C-N) (imidazole), 133.7 (N=C-NH), 126.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 123.4 (NH=C-C), 21.9 (-CH_3). EI-MS: *m/z* (%) 515 (2%), 514 (7%), 514 (4%), 513 (36%), 513 (1%), 512 (100%) base peak. Anal. calcd. (found) % for $C_{32}H_{24}ON_4S$: C, 74.98 (75.11); H, 4.72 (5.04); N, 10.93 (11.21); O, 3.12 (3.48); S, 6.26 (6.58).

General procedure for the synthesis of 2-(imino substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (6a-e):

A solution of 5 g of acetobromoglucose in 20 mL of dry acetone was added dropwise to a solution of 3 g of potassium salt of 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles in 10 mL of 5% methanolic KOH. The resulting mixture was stirred at 0 ºC for 2h. The solvent was extracted under reduced pressure after another 24 h of reaction time. TLC was used to examine the reactions. A dark syrupy mass of obtained **6a-e** was obtained.

2-(Iminobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (6a): Yield 75%, m.p.: 140 ºC. IR (KBr, ν_{max}, cm^{-1}): 3154 (NH *str.*), 3055 (CH-atom *str.*), 2855 (glucosidic C–H *str.*), 1, 755 (C=O of O-acetyl group of glycone moiety), 1, 618 (C=N *str.*), 1600 (C=C atom *str.*), 1300 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.87 (H, s, -NH), 8.88 (H, s, CH), 7.39 (H, s, imidazole-H), 6.90-8.32 (14H, m, Ar-H), 6.43 (d, anomeric proton), 1.95-2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 174.4 (N=C-S), 172.2 (s, 4C, C=O), 161.2 (CH=N), 160.5 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 121.9 (NH=C-C), 116-154 (aromatic 18 C-atom), 107.9 (s, anomeric C-atom), 22.0 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%):755 (1%), 755 (2%), 754 (12%), 754 (4%), 753 (43%), 753 (2%), 752 (100%) base peak. Anal. calcd. (found) % for $C_{39}H_{36}N_4O_{10}S$: C, 62.22 (62.28); H, 4.82 (4.86); N, 7.44 (7.49); O, 21.25 (21.28); S, 4.26 (4.29).

2-(Imino-4-chlorobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (6b): Yield 75%, m.p.: 195 ºC. IR (KBr, ν_{max}, cm^{-1}): 3140 (NH *str.*), 3044 (CH-atom *str.*), 2850 (glucosidic C–H *str.*), 1745 (C=O of O-acetyl groups of glycone moiety), 1620 (C=N *str.*), 1623 (C=C atom *str.*), 1310 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.43 (H, s, NH), 8.76 (H, s, CH), 7.46-8.13 (13H, m, Ar-H), 7.45 (H, s, imidazole-H), 6.33 (d, anomeric proton), 1.92- 2.04 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 173.3 (N=C-S), 161.2 (CH=N), 159.1 (C=C-N), 141.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 130.2 (C=C-S) (thiazole), 127-136 (aromatic 18C-atom), 115.9 (NH=C-C), 104.9 (s, anomeric C-atom), 22.5 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 790 (4%), 790 (1%), 789 (1%), 789 (16%), 788 (11%), 788 (36%), 787 (43%), 787 (1%), 786 (100%) base peak. Anal. calcd. (found) % for $C_{39}H_{35}N_4O_{10}SCl$: C, 59.50 (59.60); H, 4.48 (4.52); Cl, 4.50 (4.57); N, 7.12 (7.18); O, 20.32 (20.35); S, 4.07 (4.11).

2-(Imino-4-nitrobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazoles (6c): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3147 (NH *str.*), 3049 (CH-atom *str.*), 2858 (glucosidic C–H *str.*), 1749 (C=O of O-acetyl groups of glycone moiety), 1629 (C=N *str.*), 1629 (C=C atom *str.*), 1319 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.42 (H, s, Ar-H), 8.72 (H, s, CH), 8.29 (2H, d, Ar-H), 8.21 (H, s, imidazole-H), 6.90-8.32 (13H, m, Ar-H), 6.45 (d, anomeric proton), 1.92- 2.04 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 171.3 (N=C-S), 162.0 (CH=N), 159.1 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 126.2 (C=C-S) (thiazole), 124-150 (aromatic 18C-atom), 121.9 (NH=C-C), 105.9 (s, anomeric C-atom), 21.5 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 800 (2%), 800 (2%), 799 (9%), 799 (8%), 798 (45%), 797 (100%) base peak. Anal. calcd. (found) % for $C_{39}H_{35}N_5O_{12}S$: C, 58.71 (58.74); H, 4.42 (4.45); N, 8.78 (8.20); O, 24.07 (24.10); S, 4.02 (4.08).

2-(Imino-4-methoxybenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (6d): Yield 68%, m.p.: 212 ºC. IR (KBr, ν_{max}, cm^{-1}): 3152 (NH *str.*), 3055 (CH-atom *str.*), 2862 (glucosidic C–H *str.*), 1756 (C=O of O-acetyl groups of glycone moiety), 1634 (C=N *str.*), 1629 (C=C atom *str.*), 1325 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.48 (H, s, NH), 8.64 (H, s, CH), 8.25 (H, s, imidazole-H), 6.90-8.60 (13H, m, Ar-H), 6.54 (d, anomeric proton), 3.92 (3H, s, OCH_3), 1.92- 2.04 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 170.3 (N=C-S), 161.0 (CH=N), 158.1 (C=C-N), 141.1 (C=C-N) (imidazole), 131.8 (N=C-NH), 125.2 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 121.9 (NH=C-C), 105.4 (s, anomeric C-atom), 56.32 (-OCH_3), 21.38 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 785 (1%), 785 (2%), 784 (12%), 784 (4%), 783 (44%), 783 (1%), 782 (100%) base peak. Anal. calcd. (found) % for $C_{40}H_{38}N_4O_{11}S$: C, 61.37 (61.40); H, 4.89 (4.94); N, 7.16 (7.20); O, 22.48 (22.52); S, 4.10 (4.14).

2-(Imino-4-methylbenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1-H-imidazol-2-yl)thiazoles (6e): Yield 75%, m.p.: 227 ºC. IR (KBr, ν_{max}, cm^{-1}): 3160 (NH *str.*), 3065 (CH-atom *str.*), 2860 (glucosidic C–H *str.*), 1760 (C=O of O-acetyl groups of glycone moiety), 1643 (C=N *str.*), 1654 (C=C atom *str.*), 1343 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.88 (H, s, CH), 8.42 (H, s, imidazole-H), 6.90-8.30 (13H, m, Ar-H), 6.60 (d, anomeric proton), 2.95 (3H, s, CH_3), 1.92-2.04 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.7 (CH=N), 158.9 (C=C-N), 141.6 (C=C-N) (imidazole), 131.7 (N=C-NH), 125.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 122.4 (NH=C-C), 104.4 (s, anomeric C-atom), 22.38 (s, C-atom, CH_3 of acetyl group), 21.9 (-CH_3). EI-MS: *m/z* (%) 769 (2%), 769 (2%), 768 (11%), 768 (5%), 767 (45%), 766 (100%) base peak. Anal. calcd. (found) % for $C_{40}H_{38}N_4O_{10}S$: C, 62.65 (62.68); H, 4.99 (5.03); N, 7.31 (7.34); O, 20.86 (20.99); S, 4.18 (4.22).

General procedure for the synthesis of 2-(imino substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-imidazol-2-yl)thiazoles (6f-j): A solution of 5 g of acetobromoglucose in 20 mL of dry acetone was added dropwise to a solution of 3 g potassium salt of 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4,5-diphenylimidazol-2-yl)thiazoles in 10 mL of 5% methanolic KOH. For 2 h, the resultant mixture was stirred at 0 ºC. The solvent was extracted under reduced pressure after another 24 h of reaction time. TLC was used to evaluate the reactions. A dark syrupy mass of obtained **6f-j** was obtained.

2-(Iminobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)-thiazoles (6f): Yield 65%, m.p.: 231 ºC. IR (KBr, ν_{max}, cm^{-1}): 3156 (NH *str.*), 3065 (CH-atom *str.*), 2865 (glucosidic C–H *str.*), 1760 (C=O of O-acetyl groups of glycone moiety), 1626 (C=N *str.*), 1615 (C=C atom *str.*), 1323 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.57 (H, s, -NH), 8.98 (H, s, CH),

6.90-7.83 (19H, m, Ar-H), 6.54 (d, anomeric proton), 1.95- 2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 174.9 (N=C-S), 161.8 (CH=N), 159.9 (C=C-N), 132.8 (N=C-NH), 130.1 (C=C-N) (imidazole), 128.8 (C=C-S) (thiazole), 121.9 (NH=C-C), 120-138 (aromatic 24C-atom), 105.9 (s, anomeric C-atom), 22.9 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 827 (1%), 827 (2%), 826 (15%), 826 (4%), 825 (49%), 825 (4%), 824 (100%) base peak. Anal. calcd. (found) % for $C_{45}H_{36}N_4O_{10}S$: C, 65.52 (65.58); H, 4.40 (4.46); N, 6.79 (6.82); O, 19.40 (19.48); S, 3.89 (3.93).

2-(Imino-4-chlorobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles (6g): Yield 78%, m.p.: 198 ºC. IR (KBr, ν_{max}, cm^{-1}): 3140 (NH *str.*), 3043 (CH-atom *str.*), 2854 (glucosidic C–H *str.*), 1755 (C=O of O-acetyl groups of glycone moiety), 1636 (C=N *str.*), 1643 (C=C atom *str.*), 1345 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.42 (H, s, NH), 8.65 (H, s, CH), 6.46-7.58 (18H, m, Ar-H), 6.98 (d, anomeric proton), 1.95-2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 174.5 (N=C-S), 160.9 (CH=N), 159.8 (C=C-N), 132.5 (N=C-NH), 130.1 (C=C-N) (imidazole), 129.2 (C=C-S) (thiazole), 117-138 (arom. 24C-atom), 103.9 (s, anomeric C-atom), 21.9 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 863 (1%), 862 (5%), 862 (1%), 861 (1%), 861 (19%), 860 (14%), 860 (36%), 859 (50%), 859 (1%), 858 (100%) base peak. Anal. calcd. (found) % for $C_{45}H_{35}N_4O_{10}SCl$: C, 62.90 (62.96); H, 4.11 (4.16); Cl, 4.13 (4.18); N, 6.52 (6.58); O, 18.62 (18.69); S, 3.73 (3.78).

2-(Imino-4-nitrobenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles (6h): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3145 (NH *str.*), 3053 (CH-atom *str.*), 2865 (glucosidic C–H *str.*), 1765 (C=O of O-acetyl groups of glycone moiety), 1640 (C=N *str.*), 1654 (C=C atom *str.*), 1365 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.39 (H, s, NH), 8.41 (H, s, Ar-H), 8.72 (H, s, CH), 6.90-8.32 (18H, m, Ar-H), 6.77 (d, anomeric proton), 1.95- 2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 174.3 (N=C-S), 162.8 (CH=N), 159.8 (C=C-N), 142.1 (C=C-N) (imidazole), 133.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 124-160 (aromatic 24C-atom), 120.9 (NH-C=C), 104.9 (s, anomeric C-atom), 23.9 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 872 (3%), 872 (2%), 871 (12%), 871 (8%), 870 (51%), 869 (100%) base peak. Anal. calcd. (found) % for $C_{45}H_{35}N_5O_{12}S$: C, 62.13 (62.18); H, 4.06 (4.11); N, 8.05 (8.15); O, 22.07 (22.11); S, 3.69 (3.72).

2-(Imino-4-methoxybenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles (6i): Yield 67%, m.p.: 259 ºC. IR (KBr, ν_{max}, cm^{-1}): 3132 (NH *str.*), 3064 (CH-atom *str.*), 2832 (glucosidic C–H *str.*), 1730 (C=O of O-acetyl groups of glycone moiety), 1650 (C=N *str.*), 1675 (C=C atom *str.*), 1364 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.75 (H, s, NH), 8.85 (H, s, CH), 6.90-7.85 (18H, m, Ar-H), 7.07 (d, anomeric proton), 3.98 (3H, s, OCH_3), 1.95-2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 173.9 (N=C-S), 162.5 (CH=N), 135.3 (C=C-N), 135.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 114-165 (aromatic 24C-atom), 121.9 (NH=C-C), 103.2 (s, anomeric C-atom), 56.3 (-OCH_3), 21.9 (s, C-atom, CH_3 of acetyl group). EI-MS: *m/z* (%) 857 (2%), 857 (1%), 856 (15%), 856 (4%), 855 (51%), 855 (1%), 854 (100%) base peak. Anal. calcd. (found) % for $C_{46}H_{38}N_4O_{11}S$: C, 64.63 (64.68); H, 4.48 (4.54); N, 6.55 (6.56); O, 20.59 (20.62); S, 3.75 (3.80).

2-(Imino-4-methylbenzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazoles (6j): Yield 65%, m.p.: 276 ºC. IR (KBr, ν_{max}, cm^{-1}): 3140 (NH *str.*), 3032 (CH-atom *str.*), 2848 (glucosidic C–H *str.*), 1759 (C=O of O-acetyl groups of glycone moiety), 1687 (C=N *str.*), 1685 (C=C atom *str.*), 1354 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.82 (H, s, NH), 8.76 (H, s, CH), 6.90-7.53 (18H, m, Ar-H), 6.07 (d, anomeric proton), 2.75 (3H, s, CH_3), 1.95-2.05 (s, 4H, OAc). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.9 (CH=N), 159.9 (C=C-N), 142.6 (C=C-N) (imidazole), 133.7 (N=C-NH), 126.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 123.4 (NH=C-C), 102.9 (s, anomeric C-atom), 21.7 (s, C-atom, CH_3 of acetyl group), 21.9 (-CH_3). EI-MS: *m/z* (%) 841 (3%), 841 (2%), 840 (14%), 840 (5%), 839 (52%), 838 (100%) base peak. Anal. calcd. (found) % for $C_{46}H_{38}N_4O_{10}S$: C, 65.86 (65.94); H, 4.57 (4.62); N, 6.68 (6.75); O, 19.07 (19.14); S, 3.82 (3.88).

General procedure for the synthesis of 2-(imino substituted benzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (7a-e): To a solution of 2-(imino-substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazoles (2 g) in 25 mL of dry methanol was added 1.5 mL of 5% CH_3ONa solution. A further 24 h were spent maintaining the reaction mixture at room temperature. It was filtered, concentrated *in vacuo* and neutralized using ion exchange resin to produce a thick, very hygroscopic, brown-coloured syrupy.

2-(Iminobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (7a): Yield 65%, m.p.: 231 ºC. IR (KBr, ν_{max}, cm^{-1}): 3412 (broad, OH peak of carbohydrate residue), 3399 (NH *str.*), 2976 (CH-atom *str.*), 2954 (glucosidic C-H *str.*), 1565 (C=C atom *str.*), 1643 (C=N), 1364 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.57 (H, s, -NH), 8.98 (H, s, CH), 6.90-7.83 (14H, m, Ar-H), 5.92 (d, 1H, anomeric proton), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 174.9 (N=C-S), 161.8 (CH=N), 159.9 (C=C-N), 132.8 (N=C-NH), 130.1 (C=C-N) (imidazole), 128.8 (C=C-S) (thiazole), 121.9 (NH=C-C), 120-138 (aromatic 24C-atom), 62-109 (pyranyl 5C-atom). EI-MS: *m/z* (%) 587 (1%), 587 (2%), 586 (7%), 586 (5%), 585 (34%), 584 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{28}N_4O_6S$: C, 63.69 (63.78); H, 4.83 (4.86); N, 9.58 (9.62); O, 16.42 (16.44); S, 5.48 (5.54).

2-(Imino-4-chlorobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (7b): Yield 75%, m.p.: 195 ºC. IR (KBr, ν_{max}, cm^{-1}): 3400 (broad, OH peak of carbohydrate residue), 3398 (NH *str.*), 2970 (CH-atom *str.*), 2950 (glucosidic C-H *str.*), 1645 (C=C atom *str.*), 1632 (C=N), 1358 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.43 (H, s, NH), 8.76 (H, s, CH), 7.46-8.13 (13H, m, Ar-H), 7.45 (H, s, imidazole-H), 5.88 (d, 1H, anomeric proton), 3.51-3.98 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 173.3 (N=C-S), 161.2 (CH=N), 159.1 (C=C-N), 141.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 130.2 (C=C-S) (thiazole), 127-

136 (aromatic 18C-atom), 115.9 (NH=C-C), 60-107 (pyranyl 5C-atom). EI-MS: *m/z* (%) 622 (2%), 622 (2%), 621 (1%), 621 (13%), 620 (37%), 619 (34%), 618 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{27}N_4O_6SCl$: C, 60.14 (60.16); H, 4.40 (4.43); Cl, 5.73 (5.76); N, 9.05 (9.08); O, 15.51 (15.54); S, 5.18 (5.27).

2-(Imino-4-nitrobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (7c): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3404 (broad, OH peak of carbohydrate residue), 3401 (NH *str.*), 2975 (CH-atom *str.*), 2955 (glucosidic C-H *str.*), 1655 (C=C atom *str.*), 1642 (C=N), 1365 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.42 (H, s, Ar-H), 8.72 (H, s, CH), 8.29 (2H, d, Ar-H), 8.21 (H, s, imidazole-H), 6.90-8.32 (13H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring).^{13}C NMR (DMSO-d_6), δ ppm: 171.3 (N=C-S), 162.0 (CH=N), 159.1 (C=C-N), 142.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 126.2 (C=C-S) (thiazole), 124-150 (aromatic 18C-atom), 121.9 (NH=C-C), 58-105 (pyranyl 5C-atom). EI-MS: *m/z* (%): 632 (1%), 632 (2%), 631 (8%), 631 (4%), 630 (36%), 629 (100%) base peak. Anal. calcd. (found) % for $C_{31}H_{27}O_8N_5S$: C, 59.13 (59.17); H, 4.32 (4.36); N, 11.12 (11.20); O, 20.33 (20.48); S, 5.09 (5.13).

2-(Imino-4-methoxybenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (7d): Yield 68%, m.p.: 212 ºC. IR (KBr, ν_{max}, cm^{-1}): 3987 (broad, OH peak of carbohydrate residue), 3376 (NH *str.*), 2964 (CH-atom *str.*), 2932 (glucosidic C-H *str.*), 1630 (C=C atom *str.*), 1621 (C=N), 1350 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.48 (H, s, NH), 8.64 (H, s, CH), 8.25 (H, s, imidazole-H), 6.90-8.60 (13H, m, Ar-H), 3.92 (3H, s, OCH_3), 3.49-3.91 (m, 6H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 170.3 (N=C-S), 161.0 (CH=N), 158.1 (C=C-N), 141.1 (C=C-N) (imidazole), 131.8 (N=C-NH), 125.2 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 121.9 (NH=C-C), 62-109 (pyranyl 5C-atom), 56.32 (-OCH_3). EI-MS: *m/z* (%) 617 (1%), 617 (2%), 616 (7%), 616 (5%), 615 (35%), 615 (2%), 614 (100%) base peak. Anal. calcd. (found) % for $C_{32}H_{30}O_7N_4S$: C, 62.53 (62.55); H, 4.92 (4.98); N, 9.11 (9.14); O, 18.22 (18.32); S, 5.22 (5.26).

2-(Imino-4-methylbenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (7e): Yield 75%, m.p.: 227 ºC. IR (KBr, ν_{max}, cm^{-1}): 3975 (broad, OH peak of carbohydrate residue), 3362 (NH *str.*), 2960 (CH-atom *str.*), 2923 (glucosidic C-H *str.*), 1625 (C=C atom *str.*), 1618 (C=N), 1342 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.52 (H, s, NH), 8.88 (H, s, CH), 8.42 (H, s, imidazole-H), 6.90-8.30 (13H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring), 2.95 (3H, s, CH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.7 (CH=N), 158.9 (C=C-N), 141.6 (C=C-N) (imidazole), 131.7 (N=C-NH), 125.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 122.4 (NH=C-C), 62-109 (pyranyl 5C-atom), 21.9 (-CH_3). EI-MS: *m/z* (%) 601 (1%), 601 (2%), 600 (4%), 600 (2%), 600 (6%), 599 (37%), 598 (100%) base peak. Anal. calcd. (found) % for $C_{32}H_{30}O_6N_4S$: C, 64.20 (64.31); H, 5.05 (5.10); O, 16.03 (16.08); N, 9.36 (9.39); S, 5.36 (5.40).

General procedure for the synthesis of 2-(imino substituted benzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazoles (7f-j): To a solution of 2-(imino substituted benzal)-4-(2,3,4,6-tetra-O-acetyl-*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-imidazol-2-yl)-thiazoles (2 g) in 25 mL of dry methanol was added 1.5 mL of 5% CH_3ONa solution. A further 24 h were spent maintaining the reaction mixture at room temperature. It was filtered, concentrated *in vacuo* and neutralized using ion exchange resin to produce a thick, very hygroscopic and brown-coloured syrupy.

2-(Iminobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazole (7f): Yield 65%, m.p.: 231 ºC. IR (KBr, ν_{max}, cm^{-1}): 3410 (broad, OH peak of carbohydrate residue), 3387 (NH *str.*), 2967 (CH-atom *str.*), 2966 (glucosidic C-H *str.*), 1664 (C=N), 1570 (C=C atom *str.*), 1354 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.57 (H, s, -NH), 8.98 (H, s, CH), 6.90-7.83 (19H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 174.9 (N=C-S), 161.8 (CH=N), 159.9 (C=C-N), 132.8 (N=C-NH), 130.1 (C=C-N) (imidazole), 128.8 (C=C-S) (thiazole), 121.9 (NH=C-C), 120-138 (aromatic 24C-atom), 62-109 (pyranyl 5C-atom). EI-MS: *m/z* (%): 663 (1%), 663 (2%), 662 (9%), 662 (5%), 661 (40%), 661 (2%), 660 (100%) base peak. Anal. calcd. (found) % for $C_{37}H_{32}N_4O_6S$: C, 67.26 (67.30); H, 4.88 (4.89); N, 8.48 (8.52); O, 14.53 (14.56); S, 4.85 (4.89).

2-(Imino-4-chlorobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazole (7g): Yield 79%, m.p.: 208 ºC. IR (KBr, ν_{max}, cm^{-1}): 3402 (broad, OH peak of carbohydrate residue), 3390 (NH *str.*), 2954 (CH-atom *str.*), 2975 (glucosidic C-H *str.*), 1645 (C=N), 1577 (C=C atom *str.*), 1357 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.50 (H, s, -NH), 8.45 (H, s, CH), 6.68-7.76 (18H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 174.5 (N=C-S), 160.9 (CH=N), 159.8 (C=C-N), 132.5 (N=C-NH), 130.1 (C=C-N) (imidazole), 129.2 (C=C-S) (thiazole), 117-138 (aromatic 24C-atom), 60-110 (pyranyl 5C-atom). EI-MS: *m/z* (%) 698 (1%), 698 (3%), 697 (1%), 697 (2%), 696 (10%), 696 (36%), 695 (40%), 695 (2%), 694 (100%) base peak. Anal. calcd. (found) % for $C_{37}H_{31}N_4O_6SCl$: C, 63.93 (63.98); H, 4.49 (4.50); Cl, 5.10 (5.13); N, 8.06 (8.07); O, 13.81 (13.85); S, 4.61 (4.67).

2-(Imino-4-nitrobenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazole (7h): Yield 60%, m.p.: 159 ºC. IR (KBr, ν_{max}, cm^{-1}): 3407 (broad, OH peak of carbohydrate residue), 3398 (NH *str.*), 2962 (CH-atom *str.*), 2968 (glucosidic C-H *str.*), 1649 (C=N), 1567 (C=C atom *str.*), 1387 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.39 (H, s, NH), 8.41 (H, s, Ar-H), 8.72 (H, s, CH), 6.90-8.32 (18H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 174.3 (N=C-S), 162.8 (CH=N), 159.8 (C=C-N), 142.1 (C=C-N) (imidazole), 133.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 124-160 (aromatic 24C-atom), 120.9 (NH-C=C), 61-109 (pyranyl 5C-atom). EI-MS: *m/z* (%) 708 (1%), 708 (2%), 707 (8%), 707 (7%), 706 (43%), 705 (100%) base peak. Anal. calcd. (found) % for $C_{37}H_{31}O_8N_5S$: C, 62.97 (63.00); H, 4.43 (4.45); O, 18.14 (18.16); N, 9.92 (9.94); S, 4.54 (4.58).

2-(Imino-4-methoxybenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazole (7i):

Yield 67%, m.p.: 259 ºC. IR (KBr, ν_{max}, cm^{-1}): 3415 (broad, OH peak of carbohydrate residue), 3387 (NH *str.*), 2934 (CH-atom *str.*), 2921 (glucosidic C-H *str.*), 1634 (C=N), 1543 (C=C atom *str.*), 1358 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.75 (H, s, NH), 8.85 (H, s, CH), 6.90-7.85 (18H, m, Ar-H), 3.98 (3H, s, OCH_3), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring). ^{13}C NMR (DMSO-d_6), δ ppm: 173.9 (N=C-S), 162.5 (CH=N), 135.3 (C=C-N), 135.1 (C=C-N) (imidazole), 132.8 (N=C-NH), 129.2 (C=C-S) (thiazole), 114-165 (aromatic 24C-atom), 121.9 (NH=C-C), 62-109 (pyranyl 5C-atom), 56.3 (-OCH_3). EI-MS: *m/z* (%): 693 (1%), 693 (2%), 692 (10%), 692 (4%), 691 (41%), 691 (2%), 690 (100%) base peak. Anal. calcd. (found) % for $C_{38}H_{34}O_7N_4S$: C, 66.07 (66.08); H, 4.96 (4.99); O, 16.21 (16.24); N, 8.11 (8.16); S, 4.64 (4.68).

2-(Imino-4-methylbenzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4,5-diphenyl-1*H*-imidazole-2-yl)thiazole (7j): Yield 65%, m.p.: 276 ºC. IR (KBr, ν_{max}, cm^{-1}): 3390 (broad, OH peak of carbohydrate residue), 3333 (NH *str.*), 2933 (CH-atom *str.*), 2937 (glucosidic C-H *str.*), 1676 (C=N), 1554 (C=C atom *str.*), 1367 (C-S *str.*). ^{1}H NMR (DMSO-d_6, 400 MHz), δ ppm: 13.82 (H, s, NH), 8.76 (H, s, CH), 6.90-7.53 (18H, m, Ar-H), 3.49-3.91 (m, 4H, β-D-glucopyranosyl ring), 2.75 (3H, s, CH_3). ^{13}C NMR (DMSO-d_6), δ ppm: 170.8 (N=C-S), 161.9 (CH=N), 159.9 (C=C-N), 142.6 (C=C-N) (imidazole), 133.7 (N=C-NH), 126.6 (C=C-S) (thiazole), 115-160 (aromatic 18C-atom), 123.4 (NH=C-C), 62-109 (pyranyl 5C-atom), 21.9 (-CH_3). EI-MS: *m/z* (%) 677 (1%), 677 (2%), 676 (8%), 676 (6%), 675 (43%), 674 (100%) base peak. Anal. calcd. (found) % for $C_{38}H_{34}O_6N_4S$: C, 67.64 (67.68); H, 5.08 (5.10); O, 3.48 (3.49); N, 8.30 (8.32); S, 4.75 (4.78).

Biological activity

Antibacterial activities: The cup plate diffusion technique was used to test the synthetic compounds **3a**, **4a-b**; **5a-j** and **7a-j** for their *in vitro* antibacterial activity against *Escherichia coli*, *Klebisilla aerogens*, *Staphylococcus aureus* and *Bacillus substilis*. Ciprofloxacin and sulfacetamide (100 µg/mL), the two most common medicines, were compared to the zone of inhibition during a 24 h incubation period at 37 ºC.

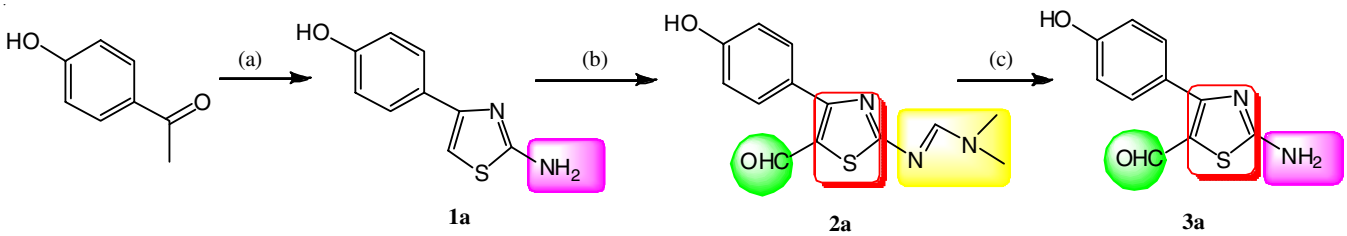
Antifungal activity: By using the cup plate diffusion technique, compounds **3a**, **4a-b**; **5a-j** and **7a-j** were further tested for their antifungal activity against *Aspergillus niger* and *Candida albicans* at a concentration of 100 µg/mL in methanol [30]. The 7 day zone of inhibition at 20 ºC was compared to 100 µg/mL doses of gentamycin and clotrimazole, as a standard drugs.

RESULTS AND DISCUSSION

Present work starts with the combination of 2-amino-4-(4-hydroxy phenyl)-1,3-thiazole (**1a**), which undergoes Vilsmeier-Haack reaction in the presence of SDS afforded intermediates **2a** and finally produce 2-amino-4-(4-hydroxy-phenyl)-1,3-thiazole-5-carboxaldehyde (**3a**). It was established that the reaction time was reduced from 4-5 h to 1-1.5 h by using a 1:1 molar concentration of SDS in the reaction medium. Sodium dodecyl sulphate is one of the least expensive, non-toxic and widely available molecules used in the Vilsmeier-Haack reaction (SDS) [31] **(Scheme-I)**.

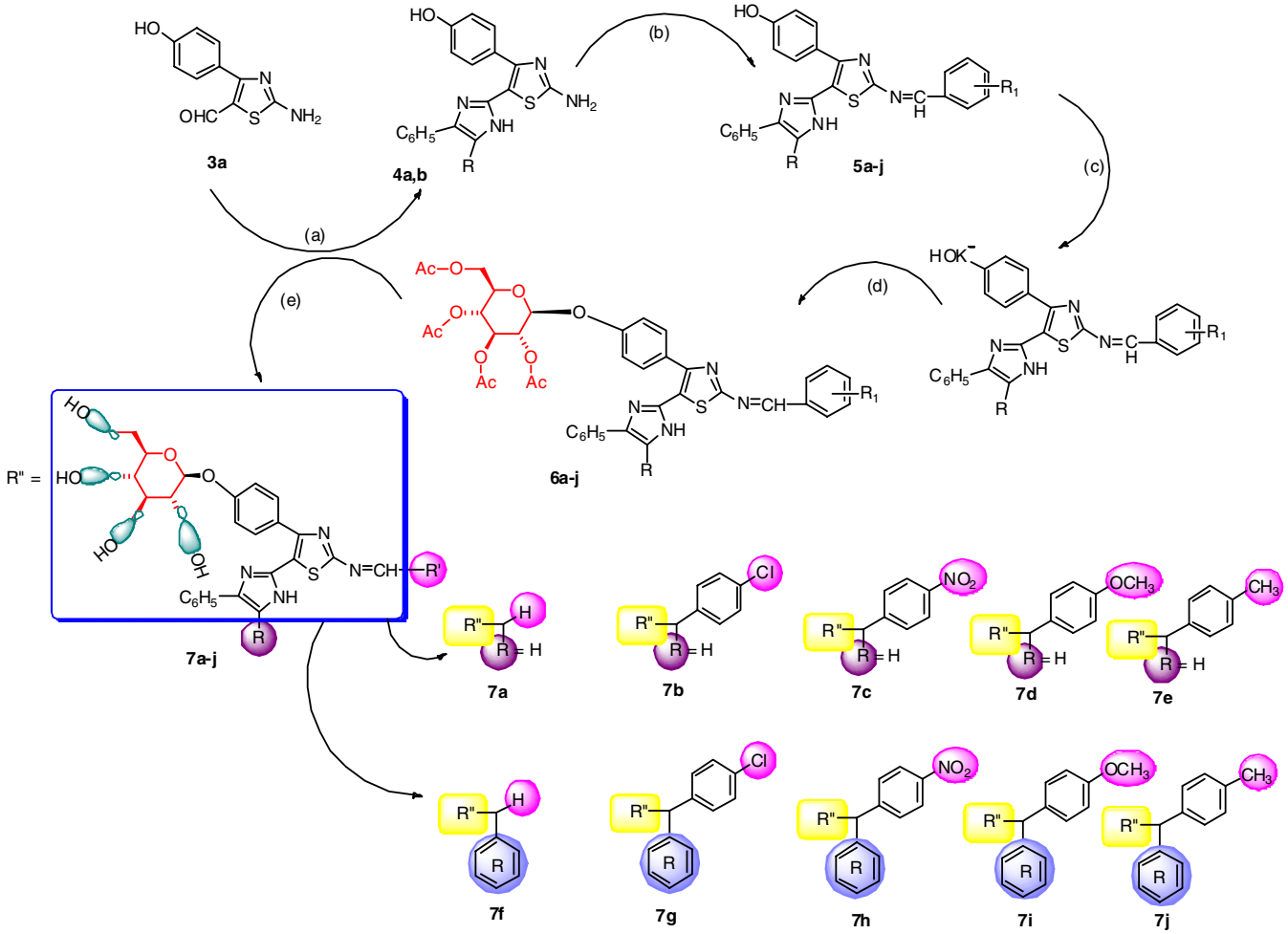
In next step, compound 4-(4-hydroxy-phenyl)-5-(4,5-substituted-1*H*-imidazol-2-yl)thiazol-2-amines (**4a-b)** [32] were synthesized by the reaction of phenyl glyoxal, ammonium acetate and glacial acetic acid with 2-amino-4-(4-hydroxy-phenyl)-1,3-thiazole-5-carboxaldehyde (**3a**). The Schiff bases were (**5a-j)** [33] synthesized from 4-(4-hydroxy-phenyl-5-(4,5-substituted-1*H*-imidazol-2-yl)thiazol-2-amine **(4a-b)** and various benzaldehydes in ethanol with a catalytic amount of glacial acetic acid. Acetobromoglucose (ACBG) was used to glucosylate 2-(imino-substituted benzal)-4-(4-hydroxy-phenyl)-5-(4,5-substituted-1*H*-imidazol-2-yl)thiazole (**5a-j**), followed by deacetylation to get the required O-glucoside with diastereoselectivity for the β-anomer. When donor's 2-hydroxyl group has an ester protecting group attached, only β-anomer by the neighbouring group participation is produced during the O-glucosylation process. Utilizing the Koeing-Knorr technique, acetobromoglucose was first made from glucose pentacetate and red phosphorus. This molecule was then reacted with potassium salts of compounds (**5a-j**) to generate 2-(imino substituted benzal) tetra-(2,3,4,6)-O-acetyl-5-(4,5-substituted-1*H*-imidazol-2-yl)thiazoles (**7a-j**). The structures of all the above synthesized molecules were confirmed by various spectroscopic analyses and a plausible mechanism is explained in **Scheme-II**.

Biological activities: As indicated in Table-1, aglycone compounds had low antimicrobial activity whereas glycosides had the maximum antibacterial activity against Gram-positive, Gram-negative bacteria and fungi. The antibacterial activity results revealed a small variance in the activities of all the glucosides against the microorganisms tested. Compounds **7a-c** and **7e-f** had the greatest antibacterial action against all the bacterial strains. Compound **7d** had low antibacterial action against all microorganisms tested. Similarly, antifungal activity data demonstrated that the glycosides had promising antifungal



1a **2a** **3a**

Scheme-I: Synthesis of 2-amino-4-(4-hydroxyphenyl)thiazole-5-carbaldehyde [Reagents and conditions: (a) thiourea, iodine, ethanol; (b) DMF, $POCl_3$, SDS, sodium carbonate; (c) NaOH/MeOH]



Scheme-II: Synthesis of 2-(imino substituted benzal)-4-(*p*-O-β-D-glucosidoxyphenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)-thiazoles [Reagents and conditions: (a) phenyl glyoxal, ammonium acetate, glacial acetic acid; (b) substituted benzaldehyde, methanol, glacial acetic acid, sodium bisulphite; (c) CH_3OH, KOH; (d) acetone, α-acetobromoglucose; (e) CH_3ONa, CH_3OH]

properties against two yeast strains (*C. albicans* and *A. niger*), except for **7d**, which showed the maximum activity against *C. albicans* but low activity against *A. niger*. These findings revealed that glycosides exhibited antibacterial properties that were both efficient and selective against studied bacteria and fungi.

Conclusion

The synthesized glucosides of 2-(imino substituted benzal)-4-(4-hydroxy-phenyl)-5-(4-phenyl-1*H*-imidazol-2-yl)thiazole (**4a**) and 2-(imino substituted benzal)-4-(4-hydroxy phenyl)-5-(4,5-diphenyl-1*H*-imidazol-2-yl)thiazole (**4b**) were evaluated for *in vitro* antimicrobial activity. The *in vitro* results indicated better pharmacological significance than that of aglycone. Particularly, we suggested that the compounds **7a-c** and **7e-f** had the greatest antibacterial action against all the bacterial strains. Only, compound **7d** had low antibacterial action against all microorganisms tested. Similarly, antifungal activity data demonstrated that the glycosides had promising antifungal properties against two yeast strains (*C. albicans* and *A. niger*), except for compound **7d**, which showed the maximum activity against *C. albicans* but low activity against *A. niger*.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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TABLE-1
ANTIMICROBIAL SCREENING RESULTS OF THE SYNTHESIZED THIAZOLE DERIVATIVES BEARING IMIDAZOLE MOIETY (**4a,b**), SCHIFF BASES (**5a-j**) AND THEIR O-GLUCOSIDES (**7a-j**)

Compound No.[a]	Zone of inhibition (mm) (Activity index) std					
	Antibacterial activity				Antifungal activity	
	Gram-positive		Gram-negative			
	S. aureus	*B. substilis*	*E. coli*	*K. aerogens*	*C. albicans*	*A. niger*
3a	17 (0.53)* (0.56)#	16 (0.57)* (0.61)#	24 (0.70)* (0.85)#	08 (0.36)* (0.38)#	20 (0.95)* (0.90)#	15 (0.62)* (0.65)#
4a	20 (0.62)* (0.66)#	21 (0.75)* (0.80)#	27 (0.79)* (0.96)#	15 (0.68)* (0.71)#	21 (1.00)* (0.95)#	16 (0.66)* (0.69)#
4b	22 (0.68)* (0.73)#	23 (0.82)* (0.88)#	26 (0.76)* (0.92)#	15 (0.56)* (0.57)#	20 (0.95)* (0.90)#	14 (0.58)* (0.60)#
5a	21 (0.65)* (0.70)#	22 (0.78)* (0.84)#	27 (0.79)* (0.96)#	16 (0.72)* (0.76)#	21 (1.00)* (0.95)#	15 (0.62)* (0.65)#
5b	25 (0.78)* (0.83)#	23 (0.82)* (0.88)#	19 (0.55)* (0.67)#	17 (0.77)* (0.81)#	16 (0.76)* (0.72)#	21 (0.87)* (0.91)#
5c	24 (0.75)* (0.80)#	23 (0.82)* (0.88)#	18 (0.52)* (0.64)#	18 (0.82)* (0.86)#	19 (0.91)* (0.86)#	19 (0.79)* (0.83)#
5d	23 (0.71)* (0.76)#	21 (0.75)* (0.80)#	19 (0.56)* (0.68)#	19 (0.86)* (0.90)#	18 (0.86)* (0.82)#	18 (0.75)* (0.78)#
5e	22 (0.68)* (0.73)#	21 (0.75)* (0.80)#	17 (0.50)* (0.60)#	18 (0.82)* (0.86)#	17 (0.80)* (0.77)#	19 (0.79)* (0.83)#
5f	25 (0.78)* (0.83)#	23 (0.82)* (0.88)#	24 (0.70)* (0.86)#	19 (0.86)* (0.90)#	21 (1.00)* (0.95)#	20 (0.83)* (0.86)#
5g	23 (0.71)* (0.76)#	22 (0.78)* (0.84)#	26 (0.76)* (0.93)#	16 (0.72)* (0.76)#	18 (0.86)* (0.82)#	16 (0.66)* (0.69)#
5h	20 (0.62)* (0.66)#	19 (0.67)* (0.73)#	20 (0.58)* (0.71)#	16 (0.72)* (0.76)#	16 (0.76)* (0.72)#	19 (0.79)* (0.83)#
5i	25 (0.78)* (0.83)#	20 (0.71)* (0.76)#	22 (0.64)* (0.78)#	19 (0.86)* (0.90)#	20 (0.95)* (0.90)#	22 (0.91)* (0.95)#
5j	30 (0.93)* (1.00)#	24 (0.85)* (0.92)#	24 (0.85)* (0.92)#	17 (0.77)* (0.80)#	18 (0.86)* (0.82)#	21 (0.87)* (0.91)#
7a	25 (0.78)* (0.83)#	24 (0.86)* (0.92)#	22 (0.65)* (0.79)#	19 (0.86)* (0.90)#	20 (0.95)* (0.91)#	22 (0.92)* (0.96)#
7b	27 (0.84)* (0.90)#	22 (0.79)* (0.85)#	23 (0.68)* (0.82)#	20 (0.91)* (0.95)#	23 (1.09)* (1.04)#	18 (0.75)* (0.78)#
7c	28 (0.87)* (0.93)#	21 (0.75)* (0.80)#	24 (0.71)* (0.86)#	18 (0.82)* (0.86)#	22 (1.04)* (1.00)#	19 (0.79)* (0.83)#
7d	26 (0.81)* (0.87)#	23 (0.82)* (0.88)#	23 (0.68)* (0.82)#	18 (0.82)* (0.86)#	21 (1.00)* (0.95)#	16 (0.67)* (0.70)#
7e	25 (0.78)* (0.83)#	24 (0.86)* (0.92)#	21 (0.62)* (0.75)#	19 (0.86)* (0.90)#	24 (1.14)* (1.09)#	18 (0.75)* (0.78)#
7f	32 (1.00)* (1.06)#	27 (0.96)* (1.04)#	25 (0.74)* (0.89)#	19 (0.86)* (0.90)#	22(1.04)* (1.00)#	20 (0.83)* (0.87)#
7g	27 (0.84)* (0.83)#	23 (0.82)* (0.88)#	27 (0.79)* (0.97)#	21 (0.95)* (1.00)#	20 (0.95)* (0.91)#	19 (0.79)* (0.83)#
7h	29 (0.91)* (0.97)#	21 (0.75)* (0.80)#	23 (0.67)* (0.82)#	18 (0.81)* (0.85)#	25 (1.19)* (1.14)#	21 (0.87)* (0.91)#
7i	27 (0.84)* (0.90)#	20 (0.71)* (0.77)#	22 (0.64)* (0.78)#	18 (0.82)* (0.86)#	19 (0.91)* (0.86)#	18 (0.75)* (0.78)#
7j	26 (0.81)* (0.87)#	28 (1.00)* (1.07)#	23 (0.68)* (0.82)#	20 (0.91)* (0.95)#	23 (1.09)* (1.04)#	19 (0.79)* (0.83)#
Std. 1	32	28	34	22	21	24
Std. 2	30	26	28	21	22	23

[a]Concentration of test compounds and standard 100 µg/mL, [b]Average zone of inhibition (mm). (Activity index) = Inhibition zone of the sample/inhibition zone of the standard, *Activity index against Std. 1, #Activity index against Std. 2; For antibacterial activity: Std. 1 = Ciprofloxacin and Std. 2 = Sulphacetamide, For antifungal activity: Std. 1 = Gentamycin and Std. 2 = Clotrimazole

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