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Synthesis, characterization and antimicrobial activity evaluation of new imidazo[2,1-*b*][1,3,4]thiadiazole derivatives

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ABSTRACT

Imidazo[2,1-*b*][1,3,4]thiadiazoles (**4a-g**) were synthesized from 3,4,5-trimethoxy benzoic acid and thiosemicarbazide. Reaction of **4** with Vilsmeier-Haack reagent yielded imidazo [2,1-*b*][1,3,4] thiadiazole–5-carbaldehyde derivatives (**5a-g**). Obtained imidazo[2,1-*b*][1,3,4] thiadia zoles-5-carbaldehydes were subjected to Knoevenagel condensation with 2-(2,4-dioxothia zolidin-3-yl)acetic acid (**1**) and 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic (**2**) in the presence of catalytic amount of piperidine and acetic acid to afford imidazo[2,1-*b*][1,3,4]thiadiazoles (**6a-g**) and (**7a-g**), respectively. The structures of the newly synthesized compounds were confirmed by IR, NMR and elemental analyses. All compounds were screened for their antibacterial and antifungal activities. Some of the compounds displayed good antibacterial and antifungal activity.

1. Introduction

Treatment of infectious diseases still remains an important and challenging problem because of a combination factors including newly emerging infectious diseases and increasing number of multi-drug resistant microbial pathogens with particular relevance for Gram-positive bacteria [1-5]. In spite of the large number of antibiotics and chemotherapeutics available for medical use, the emergence new antibiotic resistant bacterial strains in the last decades constitutes a substantial need for new class of antibacterial agents [6].

During recent years, there have been intense investigations on thiadiazole and imidazo [2,1-*b*][1,3,4]thiadiazole compounds, many of which are known to possess interesting pharmacological properties such as anticancer [7], anti-tubercular [8], antibacterial [9], antifungal [10], antimicrobial and anti-inflammatory [11,12], analgesic and antimicrobial [13], anticonvulsant, analgesic [14], and antisecretory [15] activities. Moreover, much interest has also been focused on the cardiotonic [16], diuretic [17] and herbicidal [18] activities displayed by compounds incorporating this heterocyclic system.

The varied biological activities of rhodanines (2-thioxo-thiazolidin-4-one) and their analogues have been known from the beginning of the 20th century. Rhodanines and 2,4-thiazo-lidinedione have become a pharmacologically important class of heterocyclic compounds since the introduction of various glitazones and epalrestat in to clinical use for treatment of type II diabetes and diabetic complications, respectively [19,20]. Chemical modification of these heterocycles has constantly resulted in compounds with broad spectrum of pharma-cological activities.

2,4-Thiazolidinedione derivatives constitute an important class of heterocyclic compounds for which diverse biological properties such as antibacterial and antifungal [21-24], anti-diabetic [25], cardiotonic [26], anti-oedematus and analgesic [27], cyclooxygenase and lipoxygenase inhibitory [28] activities have been documented along past decades.

In view of the high degree of bioactivity shown by the above two heterocyclic system, and initialization of our search for biological active heterocyclic compounds, it was envisaged to construct a system, which combines both these systems in a single molecular frame and to explore the additive effects towards their biological activities. Hence we are reporting herein the synthesis of imidazo [2,1-*b*][1,3,4]thiadiazole derivatives and evaluation of their antibacterial and antifungal activities.

2. Experimental

2.1. Instrumentation

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Melting points were recorded on electrothermal melting point apparatus and are uncorrected. Thin layer chromatography (TLC) controls were carried out on precoated silica gel plates (F_{254} Merck). The IR spectra were recorded on Nicolet Impact 410 FT-IR spectrophotometer using KBr pellets. ^1H and ^{13}C NMR spectra were recorded on AMX-400, Bruker-400 liquid-state NMR spectrometer using tetramethylsilane (TMS) as the internal standard. Chemical shifts were recorded as δ (ppm). Elemental analyses were carried out using a Perkin Elmer 2400-CHN Analyzer. Spectra facilities and elemental analysis were carried out by Sophisticated Analytical Instruments Facility (SAIF) division, Indian Institute of Science, Bangalore, India.

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2.2. Synthesis

2.2.1. Synthesis of 2-amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole (3)

2-amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole was obtained according to the procedure described by Al-Omar *et al.* [29] and Mazzone *et al.* [30] with a modification. A mixture of equimolar quantities of 3,4,5-trimethoxy benzoic acid (0.1 mol), thiosemicarbazide (0.1 mol) and phosphorus oxychloride (30 mL) was refluxed gently for half an hour. After cooling, water was added (90 mL) and the mixture was refluxed for 4 h and filtered. The solution was neutralized by saturated solution of potassium hydroxide. The precipitate was filtered and recrystallized from ethanol. Yield: 80%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3590, 3117, 1620. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.85 (s, 2H, -NH_2), 6.95 (d, 2H, Ar-H), 3.80 (s, 6H, OCH_3), 3.83 (s, 3H, OCH_3).

2.2.2. General Procedure: synthesis of 2-(3,4,5-trimethoxy phenyl) 6-(4'substituted aryl) imidazo[2,1-b][1,3,4]-thiadiazoles (4a-g)

2-(3,4,5-trimethoxyphenyl)6-(4'substituted aryl) imidazo [2,1-b][1,3,4]-thiadiazoles were obtained according to the procedure described by Mazzone *et al.* [30] with a modification. A mixture of equimolar quantities of 2-amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole (0.01 mol) and an appropriate α-bromoketones (0.01 mol) was refluxed in dry ethanol (300 mL) for 10 h. Excess of solvent was removed under reduced pressure the solid hydrobromide salts suspended in water, and neutralized by aqueous sodium carbonate solution to get free base. It was filtered, washed with water, dried, and recrystallized from suitable solvent.

2-(3,4,5-trimethoxyphenyl)-6-phenylimidazo[2,1-b][1,3,4] thiadiazole (**4a**): Yield: 70%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3095, 3033, 2943, 1576, 1490, 1339, 1130, 843. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.75 (s, 1H, H-5 imidazole), 7.40 (m, 5H, Ar-H), 7.41 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.70 (s, 3H, OCH_3).

2-(3,4,5-trimethoxyphenyl)-6-(4-methylphenyl)-imidazo[2,1-b][1,3,4] thiadiazole (**4b**): Yield: 71 %. M.p.: 136-137 °C. IR (KBr, cm^{-1}): 3090, 3025, 2947, 1586, 1489, 1329, 1130, 839. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.64 (s, 1H, H-5 imidazole), 7.77 (d, 2H, Ar-H), 7.22 (d, 2H, Ar-H), 7.14 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3), 3.29 (s, 3H, CH_3).

2-(3,4,5-trimethoxyphenyl)-6-(4-methoxyphenyl)-imidazo [2,1-b][1,3,4] thiadiazole (**4c**): Yield: 70%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3085, 3043, 2973, 1596, 1481, 1343, 1150, 843. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.46 (s, 1H, H-5 imidazole), 7.62 (d, 2H, Ar-H), 7.42 (d, 2H, Ar-H), 7.14 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3).

2-(3,4,5-trimethoxyphenyl)-6-(4-nitrophenyl)-imidazo[2,1-b][1,3,4] thiadiazole (**4d**): Yield: 70%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3060, 3021, 2959, 1587, 1494, 1346, 1128, 853. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.85 (s, 1H, H-5 imidazole), 8.40 (d, 2H, Ar-H), 8.16 (d, 2H, Ar-H), 8.04 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.70 (s, 3H, OCH_3).

2-(3,4,5-trimethoxyphenyl)-6-(4-bromophenyl)-imidazo[2,1-b][1,3,4] thiadiazole (**4e**): Yield: 70%. M.p.: 188-190 °C. IR (KBr, cm^{-1}): 3095, 3043, 2944, 1586, 1490, 1329, 1130, 833. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.74 (s, 1H, H-5 imidazole), 8.30 (d, 2H, Ar-H), 8.15 (d, 2H, Ar-H), 8.07 (d, 2H, Ar-H), 3.90 (s, 6H, OCH_3), 3.75 (s, 3H, OCH_3).

2-(3,4,5-trimethoxyphenyl)-6-(4-chlorophenyl)-imidazo[2,1-b][1,3,4] thiadiazole (**4f**): Yield: 70%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3075, 3053, 2933, 1566, 1490, 1359, 1128, 833. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.76 (s, 1H, H-5 imidazole), 7.89 (d, 2H, Ar-H), 7.49 (d, 2H, Ar-H), 7.41 (d, 2H, Ar-H), 3.90 (s, 6H, OCH_3), 3.75 (s, 3H, OCH_3).

2-(3,4,5-trimethoxyphenyl)-6-(6-(2,5-methoxyphenyl)imid azo[2,1-b] [1,3,4] thiadiazole (**4g**): Yield: 70%. M.p.: 205-208 °C. IR (KBr, cm^{-1}): 3095, 3055, 2983, 1576, 1480, 1339, 1130, 843. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 8.56 (s, 1H, H-5 imidazole), 7.65 (m, 3H, Ar-H), 7.24 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3).

2.2.3. General procedure for the synthesis of 6-Aryl-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (5a–g)

Vilsmeier-Haak reagent was prepared by adding phosphoryl chloride (3 mL), in dimethylformamide (20 mL), at 0 °C with stirring. Then appropriately substituted arylimidazo [2,1-*b*][1,3,4]thiadiazole (**4a-g**) (0.01 mol) was added to the reagent and stirred at 0 °C for 30 min. The mixture was further stirred for 2h at room temperature and at 60 °C for additional 2 h. the reaction mixture was then poured in sodium carbonate solution and stirred at 90 °C for 2 h. After cooling, the mixture was diluted with water, extracted with chloroform, and collective extract was washed with water and dried over anhydrous sodium sulphate. The residue obtained after the removal of chloroform was recrystallized from suitable solvent to get the crystalline solid.

6-phenyl-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4] thiadiazole-5-carbaldehyde (**5a**): Yield: 70%. Dark brown crystal. M.p.: 180-182 °C. IR (KBr, cm^{-1}): 3016, 2840, 2737, 1674, 1130, 732. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 10.09 (s, 1H, CHO), 7.60 (m, 5H, Ar-H), 7.23 (d, 2H, Ar-H), 3.91 (s, 6H, OCH_3), 3.89 (s, 3H, OCH_3).

6-(4-methylphenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**5b**): Yield: 70%. Colourless crystals. M.p.: 145-148 °C. IR (KBr, cm^{-1}): 3089, 2892, 2765, 1677, 1130, 798. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 10.05 (s, 1H, CHO), 7.88 (d, 2H, Ar-H), 8.33 (d, 2H, Ar-H), 7.22 (d, 2H, Ar-H), 3.89 (s, 6H, OCH_3), 3.76 (s, 3H, OCH_3), 3.29 (s, 3H, CH_3).

6-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)imidazo [2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**5c**): Yield: 70%. Brownish product. M.p.: 155-157 °C. IR (KBr, cm^{-1}): 3087, 2940, 2860, 2798, 1680, 1201, 1167, 823. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 10.08 (s, 1H, CHO), 7.67 (d, 2H, Ar-H), 8.43 (d, 2H, Ar-H), 7.24 (d, 2H, Ar-H), 3.90 (s, 6H, OCH_3), 3.74 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3).

6-(4-nitrophenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4] thiadiazole-5-carbaldehyde (**5d**): Yield: 70%. Brownish-yellow crystals. M.p.: 175-176 °C. IR (KBr, cm^{-1}): 3056, 2976, 2835, 2787, 1674, 1204, 1354, 798. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 9.55 (s, 1H, CHO), 7.86 (d, 2H, Ar-H), 8.43 (d, 2H, Ar-H), 7.21 (d, 2H, Ar-H), 3.88 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3).

6-(4-bromophenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4] thiadiazole-5-carbaldehyde (**5e**): Yield: 70%. Light brown crystals. M.p.: 195-196 °C. IR (KBr, cm^{-1}): 3050, 2945, 2854, 2789, 1680, 1167, 843, 788. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 9.43 (s, 1H, CHO), 8.29 (d, 2H, Ar-H), 8.15 (d, 2H, Ar-H), 7.20 (d, 2H, Ar-H), 3.87 (s, 6H, OCH_3), 3.75 (s, 3H, OCH_3).

6-(4-chlorophenyl)-2-(3, 4, 5-trimethoxyphenyl)imidazo[2,1-b][1,3,4] thiadiazole-5-carbaldehyde (**5f**): Yield: 70%. Dark brown crystals. M.p.: 176-178 °C. IR (KBr, cm^{-1}): 3056, 2894, 2793, 1673, 1203, 1156, 785. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 10.09 (s, 1H, CHO), 8.06 (d, 2H, Ar-H), 7.60 (d, 2H, Ar-H), 7.24 (d, 2H, Ar-H), 3.91 (s, 6H, OCH_3), 3.89 (s, 3H, OCH_3).

6-(2,5-dimethoxyphenyl)-2-(3,4,5-trimethoxyphenyl)imidazo [2,1-b][1,3,4] thiadiazole-5-carbaldehyde (**5g**): Yield: 70%. brownish product M.p.: 177-178 °C. IR (KBr, cm^{-1}): 3076, 2914,

2773, 1669, 1234, 1136, 775. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 10.06 (s, 1H, CHO), 7.57 (m, 3H, Ar-H), 7.24 (d, 2H, Ar-H), 3.90 (s, 6H, OCH_3), 3.74 (s, 3H, OCH_3), 3.50 (s, 3H, OCH_3), 3.47 (s, 3H, OCH_3).

2.2.4. General procedure for the synthesis of 2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-b][1,3,4] thiadiazol-5-yl) methylene)-2,4-dioxothiazolidin-3-yl) acetic acid 6a-g

A mixture of the 6-Aryl-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-*b*][1,3,4]thiadiazole-5-carbaldehyde (**5a–g**) (0.001 mol), 2-(2,4-dioxothiazolidin-3-yl)acetic acid [31] (0.001 mol), piperidine (0.001 mol) and acetic acid (0.001 mol) in toluene (50 mL) was heated under reflux with azeotropic removal of water for 16 h. The mixture was cooled to 5 °C; filtration gave crude 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo [2,1-*b*][1,3,4]thiadiazol-5-yl)methylene)-2, 4-dioxothiazolidin-3-yl) acetic acid. The crude product was recrystallized from appropriate solvents.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-phenylimidazo[2,1-b][1,3,4] thiadiazol-5-yl) methylene)-2,4-dioxothiazolidin-3-yl) acetic acid (**6a**): Yield: 77%. Light yellow solid. M.p.: 191-193 °C. IR (KBr, cm^{-1}): 3363, 3042, 2953, 1720, 1704, 1660, 1320, 1156. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.65 (br s, 1H, COOH), 7.90 (d, 2H, Ar-H), 7.87 (s, 1H, -CH=C), 7.48 (m, 5H, Ar-H), 4.69 (s, 2H, CH_2), 3.90 (s, 6H, OCH_3), 3.89 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 169.45, 168.23, 164.12, 150.65, 149.34, 139.78, 135.82, 133.54, 130.36, 128.48, 127.87, 126.32, 124.38, 121.43, 120.82, 114.37, 57.73, 55.35, 42.17. Anal. Calcd. for ($C_{25}H_{20}N_4O_7S_2$) (%): C, 54.34; H, 3.65; N, 10.14. Found; C, 54.32; H, 3.63; N, 10.15.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-p-tolylimidazo [2,1-b][1,3,4] thiadiazol-5-yl) methylene)-2,4-dioxothiazolidin-3-yl) acetic acid (**6b**): Yield: 75%, light yellow solid. M.p.: 184-186 °C. IR (KBr, cm^{-1}): 3384, 3056, 2976, 1720, 1698, 1671, 1615, 1330, 1166. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.42 (br s, 1H, COOH), 8.76 (d, 2H, Ar-H), 7.83 (s, 1H, CH=C), 7.65 (m, 2H, Ar-H), 7.18 (m, 2H, Ar-H), 4.68 (s, 2H, CH_2), 3.89 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3), 3.29 (s, 3H, CH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 170.69, 169.86, 160.88, 152.12, 149.78, 140.39, 138.27, 133.86, 133.26, 129.34, 128.74, 126.02, 124.83, 117.53, 116.64, 115.77, 56.93, 55.46, 43.42, 30.19. Anal. Calcd. for ($C_{26}H_{22}N_4O_7S_2$) (%): C, 55.11; H, 3.91; N, 9.89. Found; C, 55.06; H, 3.89; N, 9.87.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-(4-methoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-2,4-dioxothiazo lidin-3-yl) acetic acid (**6c**): Yield: 50%. Yellow solid. M.p.: 211-213 °C. IR (KBr) cm^{-1}: 3392, 3071, 2955, 1726, 1700, 1670, 1620, 1340, 1150. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.51 (br s, 1H, COOH), 8.95 (d, 2H, Ar-H), 8.15 (m, 2H, Ar-H), 7.84 (s, 1H, CH=C), 7.65 (m, 2H, Ar-H), 4.70 (s, 2H, CH_2), 3.91 (s, 6H, OCH_3), 3.88 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 171.42, 167.16, 166.31, 151.63, 148.52, 141.28, 138.53, 133.33, 133.24, 132.70, 129.52, 126.65, 125.92, 121.29, 116.83, 116.62, 58.46, 56.46, 45.19, 43.64. Anal. Calcd. for ($C_{26}H_{22}N_4O_8S_2$) (%): C, 53.60; H, 3.81; N, 9.62. Found; C, 53.58; H, 3.75; N, 9.65.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-(4-nitrophenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-2,4-dioxo thiazolidin-3-yl) acetic acid (**6d**): Yield: 59%. Yellow powder. M.p.: 191-192 °C. IR (KBr, cm^{-1}): 3373, 3064, 2856, 1725, 1698, 1675, 1619, 1318, 1170. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.44 (br s, 1H, COOH), 8.19 (d, 2H, Ar-H), 7.85 (s, 1H, CH=C), 7.63 (d, 2H, Ar-H), 7.14 (d, 2H, Ar-H), 4.72 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.84 (s, 6H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 170.33, 167.87, 166.20, 150.12, 147.23, 142.31, 138.29, 132.11, 131.42, 129.87, 128.65, 124.39, 123.08, 121.78, 120.42, 113.26, 57.46, 4561, 43.55. Anal. Calcd. for ($C_{25}H_{19}N_5O_9S_2$) (%): C, 50.25; H, 3.20; N, 11.72. Found; C, 50.20; H, 3.17; N, 11.70.

2-((5Z)-5-((6-(4-bromophenyl)-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-2,4-dioxothia zolidin-3-yl) acetic acid (**6e**): Yield: 59%. Yellow solid. M.p.: 219-220 °C. IR (KBr, cm^{-1}): 3356, 3072, 2873, 1728, 1695, 1665, 1613, 1325, 1149. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.89 (br s, 1H, COOH), 8.65 (d, 2H, Ar-H), 7.83 (s, 1H, CH=C), 7.56 (d, 2H, Ar-H), 7.38 (d, 2H, Ar-H), 4.72 (s, 2H, CH_2), 3.87 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 169.37, 168.26, 166.02, 151.73, 149.91, 141.27, 134.87, 132.52, 130.69, 130.12, 129.83, 128.42, 128.12, 125.87, 120.89, 112.38, 59.51, 45.17, 43.68. Anal. Calcd. for ($C_{25}H_{19}BrN_4O_7S_2$) (%): C, 47.55; H, 3.03; N, 8.87. Found; C, 47.51; H, 3.01; N, 8.83.

2-((5Z)-5-((6-(4-chlorophenyl)-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-2,4-dioxothia zolidin-3-yl) acetic acid (**6f**): Yield: 54%. Yellow solid. M.p.: 214-215 °C. IR (KBr) cm^{-1}. 3339, 3064, 2896, 1720, 1698, 1660, 1620, 1334, 1138. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.86 (br s, 1H, COOH), 8.36 (d, 2H, Ar-H), 7.98 (s, 1H, CH=C), 7.91 (d, 2H, Ar-H), 7.41 (d, 2H, Ar-H), 4.75 (s, 2H, CH_2), 3.90 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 167.73, 167.07, 166.57, 150.37, 148.25, 139.19, 137.34, 131.48, 130.38, 129.29, 127.96, 125.28, 124.19, 121.17, 120.17, 118.18, 59.79, 45.03, 44.77. Anal. Calcd. for ($C_{25}H_{19}ClN_4O_7S_2$) (%): C, 41.15; H, 3.26; N, 9.54. Found; C, 41.10; H, 3.23; N, 9.56.

2-((5Z)-5-((6-(2,5-dimethoxylphenyl)-2-(3,4,5-trimethoxy phenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-2,4-dioxothiazolidin-3-yl) acetic acid (**6g**): Yield: 52%. Yellow solid. M.p.: 221-223 °C. IR (KBr, cm^{-1}): 3373, 3061, 2925, 1720, 1700, 1673, 1629, 1332, 1141. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 12.95 (br s, 1H, COOH), 8.20 (d, 2H, Ar-H), 8.03 (m, 1H, Ar-H), 7.73 (s, 1H, CH=C), 7.64 (m, 2H, Ar-H), 4.72 (s, 2H, CH_2), 3.87 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 170.53, 167.38, 166.51, 151.16, 147.27, 141.47, 137.53, 133.26, 131.42, 129.87, 128.38, 127.52, 126.39, 125.46, 119.78, 113.70, 112.28, 56.46, 55.44, 54.36, 53.97, 39.17. Anal. Calcd. for ($C_{27}H_{24}N_4O_9S_2$) (%): C, 52.93; H, 3.95; N, 9.15. Found; C, 52.90; H, 3.90; N, 9.17.

2.2.5. General procedure for the synthesis of 2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo [2,1-b][1,3,4] thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) acetic acid (7a-g)

A mixture of the 6-Aryl-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-*b*][1,3,4]thiadiazole-5-carbaldehyde (**5a-g**) (0.001 mol), 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid (0.001 mol), piperidine (0.001 mol) and acetic acid (0.001 mol) in toluene (50 mL) was heated under reflux with azeotropic removal of water for 16 h. The mixture was cooled to 5 °C; filtration gave crude 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo [2,1-*b*][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazo lidin-3-yl) acetic acid. The crude product was recrystallized from appropriate solvents.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-phenylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) acetic acid (**7a**): Yield: 61%. Yellow solid. M.p.: 211-213 °C. IR (KBr, cm^{-1}): 3263, 3052, 2831, 1720, 1681, 1320, 1156, 790. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.90 (br s, 1H, COOH), 8.08 (d, 2H, Ar-H), 7.76 (s, 1H, CH=C), 7.59 (m, 5H, Ar-H), 4.61 (s, 2H, CH_2), 3.91 (s, 6H, OCH_3), 3.88 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 193.05, 167.21, 166.41, 161.68, 150.87, 149.30, 139.54, 136.59, 134.12, 131.82, 129.23, 127.92, 126.61, 124.83, 121.32, 120.41, 114.32, 57.31, 55.58, 45.19. Anal. Calcd. for ($C_{25}H_{20}N_4O_6S_3$) (%): C, 52.81; H, 3.55; N, 9.85. Found; C, 52.78; H, 3.50; N, 9.86.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-p-tolylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-

yl) acetic acid (**7b**): Yield: 60%. Light yellow solid. M.p.: 196-198 °C. IR (KBr, cm^{-1}): 3354, 3056, 2976, 2858.21, 1720, 1671, 1612, 1323, 1153, 981. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.32 (br s, 1H, COOH), 8.21 (d, 2H, Ar-H), 7.77 (s, 1H, CH=C), 7.15 (d, 2H, Ar-H), 6.95 (d, 2H, Ar-H), 4.67 (s, 2H, CH_2), 3.90 (s, 3H, OCH_3), 3.89 (s, 6H, OCH_3), 3.63 (s, 3H, CH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 193.00, 167.18, 166.44, 151.53, 149.07, 140.72, 137.63, 136.49, 130.43, 127.06, 126.31, 125.58, 123.39, 121.51, 119.73, 113.69, 112.28, 55.75, 45.62, 43.52, 22.16. Anal. Calcd. for ($C_{26}H_{22}N_4O_6S_3$) (%): C, 53.60; H, 3.81; N, 9.62. Found; C, 53.57; H, 3.76; N, 9.60.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-(4-methoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxo thiazolidin-3-yl) acetic acid (**7c**): Yield: 50%. Yellow solid. M.p.: 206-208 °C. IR (KBr, cm^{-1}): 3392, 3071, 2955, 2868, 1726, 1670, 1627, 1324, 1145, 967. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.29 (br s, 1H, COOH), 8.41 (d, 2H, Ar-H), 7.93 (s, 1H, CH=C), 7.88 (d, 2H, Ar-H), 7.80 (d, 2H, Ar-H), 4.72 (s, 2H, CH_2), 3.90 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 193.18, 167.17, 166.33, 159.71, 147.32, 140.86, 137.76, 134.18, 133.62, 130.33, 129.75, 126.43, 122.86, 122.22, 117.20, 115.79, 55.39, 45.47, 43.57, 40.13. Anal. Calcd. for ($C_{26}H_{22}N_4O_7S_3$) (%): C, 52.16; H, 3.70; N, 9.36. Found; C, 52.12; H, 3.68; N, 9.34.

2-((5Z)-5-((2-(3,4,5-trimethoxyphenyl)-6-(4-nitrophenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thio xothiazolidin-3-yl) acetic acid (**7d**): Yield: 52%. Yellow solid. M.p.: 223-225 °C. IR (KBr) cm^{-1}: 3382, 3071, 2934, 2856, 1727, 1675, 1613, 1323, 1170, 982. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.27 (br s, 1H, COOH), 8.16 (d, 2H, Ar-H), 7.78 (s, 1H, CH=C), 7.65 (d, 2H, Ar-H), 7.34 (d, 2H, Ar-H), 4.68 (s, 2H, CH_2), 3.89 (s, 3H, OCH_3), 3.87 (s, 6H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 192.47, 167.05, 166.18, 151.73, 147.93, 141.53, 134.20, 133.37, 132.84, 129.20, 127.92, 126.55, 125.43, 122.50, 119.57, 113.28, 57.26, 46.75, 43.76. Anal. Calcd. for ($C_{25}H_{19}N_5O_8S_3$) (%): C, 48.93; H, 3.12; N, 11.41. Found; C, 34.90; H, 3.10; N, 11.43.

2-((5Z)-5-((6-(4-bromophenyl)-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxo thiazolidin-3-yl) acetic acid (**7e**): Yield: 61%. Yellow solid. M.p.: 231-232 °C. IR (KBr, cm^{-1}): 3372, 3072, 2947, 2873, 1720, 1678, 1625, 1337, 1129, 978. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.22 (br s, 1H, COOH), 8.14 (d, 2H, Ar-H), 7.70 (s, 1H, CH=C), 7.25 (d, 2H, Ar-H), 6.80 (d, 2H, Ar-H), 4.63 (s, 2H, CH_2), 3.91 (s, 3H, OCH_3), 3.90 (s, 6H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 192.75, 167.02, 166.26, 157.93, 149.32, 140.73, 136.65, 131.75, 130.33, 129.27, 127.38, 126.11, 123.23, 117.81, 117.27, 109.18, 57.68, 45.32, 43.23. Anal. Calcd. for ($C_{25}H_{19}BrN_4O_6S_3$) (%): C, 46.37; H, 2.96; N, 8.65. Found; C, 46.34; H, 2.92; N, 8.63.

2-((5Z)-5-((6-(4-chlorophenyl)-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thi oxothiazolidin-3-yl) acetic acid (**7f**): Yield: 54%. Yellow solid. M.p.: 214-215 °C. IR (KBr, cm^{-1}): 3339, 3064, 2896, 1720, 1698, 1660, 1620, 1334, 1138. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.36 (br s, 1H, COOH), 8.16 (d, 2H, Ar-H), 7.85 (s, 1H, CH=C), 7.49 (d, 2H, Ar-H), 7.21 (d, 2H, Ar-H), 4.67 (s, 2H, CH_2), 3.90 (s, 6H, OCH_3), 3.89 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 192.47, 167.05, 166.18, 150.37, 147.93, 139.19, 137.34, 134.28, 133.23, 132.69, 129.75, 127.28, 126.74, 125.52, 119.25, 113.18, 59.79, 45.72, 43.54. Anal. Calcd. for ($C_{25}H_{19}ClN_4O_6S_3$) (%): C, 49.79; H, 3.18; N, 9.29. Found; C, 49.75; H, 3.16; N, 9.27.

2-((5Z)-5-((6-(2,5-dimethoxylphenyl)-2-(3,4,5-trimethoxy phenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) acetic acid (**7g**): Yield: 52%. Yellow solid. M.p.: 213-215 °C. IR (KBr, cm^{-1}): 3373, 3061, 2925, 2845, 1724, 1681, 1620, 1362, 1134, 968. ^{1}H NMR (400 MHz, δ, ppm, DMSO-d_6): 13.32 (br s, 1H, COOH), 8.38 (d, 2H, Ar-H), 7.92 (s, 1H, CH=C), 7.65 (m, 3H, Ar-H), 4.67 (s, 2H, CH_2), 3.90 (s, 6H, OCH_3), 3.89 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3). ^{13}C NMR (400 MHz, δ, ppm, DMSO-d_6): 192.29, 166.95, 165.81, 150.74, 146.70, 140.66, 137.22, 132.29, 131.78, 128.54, 126.21, 123.83, 120.47, 119.28, 117.69, 114.36, 56.33, 50.49, 45.74, 43.57. Anal. Calcd. for ($C_{27}H_{24}N_4O_8S_3$) (%): C, 51.58; H, 3.85; N, 8.91. Found; C, 51.55; H, 3.83; N, 8.90.

2.3. Microbiology

For the antibacterial and antifungal activity, the compounds were dissolved in dimethylsulfoxide (DMSO). Further dilutions of the compounds and standard drugs in the test medium were prepared at the required quantities of 128, 64, 32, 16, 8, 4, 2, 1 µg/mL concentrations with Mueller-Hinton broth and Sabouraud dextrose broth. The minimum inhibitory concentrations (MIC) were determined using the twofold serial dilution technique [32]. A control test was also performed containing inoculated broth supplemented with only DMSO at the same dilutions used in our experiments and found inactive in the culture medium. All the compounds were tested for their in vitro growth inhibitory activity against different bacteria and fungi, Ampicillin and Kanamycin were used as the reference standard for antibacterial activity while ketoconazole was used as the reference standard for antifungal activity, the MIC value were summarized in Table 1.

The cultures were obtained from Mueller-Hinton broth for all the bacterial strains after 24 h of incubation at 37 ± 1 °C. Fungi were maintained in Sabouraud dextrose broth after incubation for 24 h at 25 ± 1 °C. Testing was carried out in Mueller-Hinton broth and Sabouraud dextrose broth at pH 7.4 and the twofold serial dilution technique was applied. The final inoculum's size was 10^5 CFU/mL for the antibacterial assay and 10^4 CFU/mL for the antifungal assay. A set of tubes containing only inoculated broth was used as controls. For the antibacterial assay after incubation for 24 h at 37±1 °C and after incubation for 48 h at 25 ± 1°C for antifungal assay, the tube with no growth of microorganism was recorded to represent the MIC expressed in µg/mL. Every experiment in the antibacterial and antifungal assays was replicated twice.

3. Results and discussion

3.1. Synthesis

The synthetic route of the compounds (**6a-g** and **7a-g**) is outlined in Scheme 1. The 2-(2,4-dioxothiazolidin-3-yl)acetic acid (**1**) was prepared according to earlier reported method [31] and 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic (**2**) acid is available commercial (Figure 1).

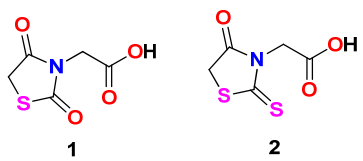


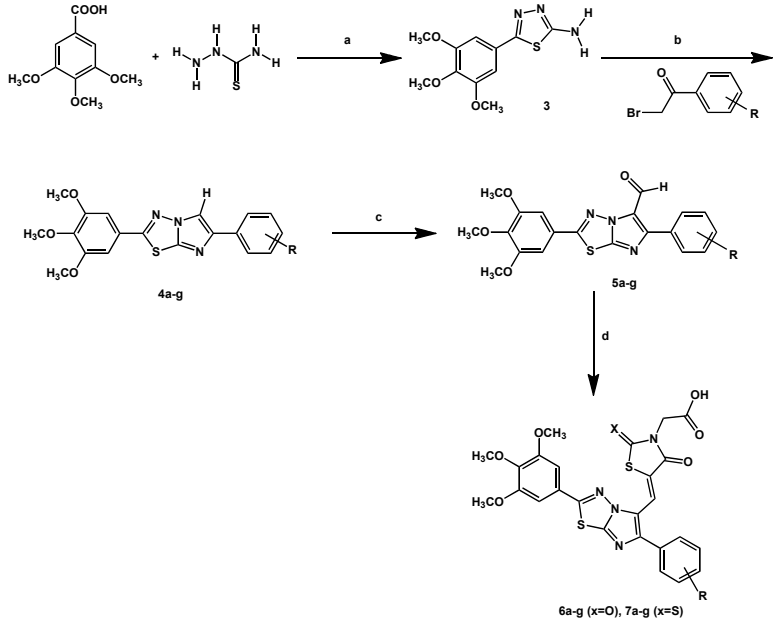
Figure 1. (1) 2-(2,4-dioxothiazolidin-3-yl)acetic acid; (2) 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid.

2-Amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole (**3**) was obtained by direct cyclisation of a 3,4,5-trimethoxy benzoic acid and thiosemicarbazide in the presence of phosphorus oxychloride, the latter refluxed with substituted α-haloaryl ketones in dry ethanol yielded the imidazothiadiazoles (**4a-g**) in good yield. It is well established that this reaction proceeds via the intermediate iminothiadiazole [9], which undergoes

Table1. Results of antibacterial and antifungal activities of compounds (**6a-g** and **7a-g**) [minimum inhibitory concentration (MIC in µg/mL) values (mean of triplicates)]*.

Compound	R	*E.c*	*P.a*	*S.a*	*E.f*	*C.a*	*C.n*	*A.f*	*A.n*
6a	H	128	128	128	64	64	64	64	128
6b	4-CH_3	128	128	128	64	64	64	128	128
6c	4-OCH_3	128	128	128	64	64	64	64	32
6d	4-NO_2	128	128	128	128	64	64	64	128
6e	4-Br	128	128	16	16	16	16	16	32
6f	4-Cl	128	128	32	32	16	16	16	16
6g	2,5-(OCH_3)	128	128	128	128	64	64	64	64
7a	H	128	64	64	64	32	32	16	16
7b	4-CH_3	64	64	64	64	64	64	32	64
7c	4-OCH_3	128	64	64	64	32	64	32	64
7d	4-NO_2	128	128	64	64	64	32	64	64
7e	4-Br	32	32	4	8	4	8	4	4
7f	4-Cl	64	32	16	8	8	8	8	4
7g	2,5-(OCH_3)	64	64	64	64	32	32	64	16
Ampicillin	-	2	2	NT	NT	NT	NT	NT	NT
Kanamycin	-	NT	NT	2	1	NT	NT	NT	NT
Ketoconazole	-	NT	NT	NT	NT	2	1	2	1

**NT: not tested.; E.c: Escherichia coli.; P.a: Pseudomonas aeruginosa.; S.a: Staphylococcus aureus.; E.f: Enterococcus faecalis.; C.a: Candida albicans.; C.n: Cryptococcus neoformans.; A.f: Aspergillus flavus.; A.n: Aspergillus niger.*



Reagents: (a) phosphorus oxychloride; (b) dry ethanol; (c) dimethylformamide, phosphorus oxychloride (Vilsmeiere-Haack reagent); (d) 2-(2,4-dioxothiazolidin-3-yl)acetic acid. 2-(4-oxo-2-thioxothiazolidin-3-yl) acetic acid, piperidine, acetic acid, toluene.

Scheme 1

dehydrocyclisation to form the desired fused heterocycle under reflux temperature spontaneously. The electronic and steric factors at 5th position of 2-amino-5-substituted-1,3,4-thiadiazole are crucial in determining the course of its reaction with substituted α-haloaryl ketones. The strongly electronegative groups impart less nucleophilic character to the nitrogen at 4th position of the 1,3,4-thiadiazole. Various α-haloaryl ketones were prepared by the bromination of the corresponding ketones.

Vilsmeier-Haack reaction of imidazo[2,1-*b*][1,3,4] thiadiazoles (**4a-g**) in dimethylformamide and phosphorus oxychloride provided 6-aryl-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-*b*][1,3,4]thiadiazole–5-carbaldehyde derivatives (**5a-g**). Thus obtained imidazo[2,1-*b*][1,3,4]thiadiazoles-5-carbaldehydes (**5a-g**) were subjected to Knoevenagel condensation with 2-(2,4-dioxothiazolidin-3-yl)acetic acid (**1**) and 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid (**2**) in the presence of catalytic amount of piperidine and acetic acid to afford imidazo[2,1-*b*][1,3,4]thiadiazoles (**6a-g**) and (**7a-g**), respectively.

The formation of 2-aminothiadiazole (**3**) by the reaction between 3,4,5-trimethoxy benzoic acid and thiosemicarbazide was confirmed by IR spectra, which showed the presence of amine (–NH_2) band and absence of carbonyl stretching of carboxylic acid. Structures of imidazothiadiazole derivatives (**4a-g**) were established by the absence of amine (–NH_2) band in IR spectra and appearance of imidazole proton (H-5) around δ 8.6 in the ^{1}H NMR spectra. IR spectra of aldehydes (**5a-g**) displayed a sharp band for carbonyl stretching frequency ($\nu_{C=O}$) around 1680 cm^{-1} and the signal for imidazole proton (H-5) in ^{1}H NMR spectrum was absent. A new signal for aldehyde proton was observed around δ: 10.00 ppm in the ^{1}H NMR spectra, thus substantiating the formation of imidazo[2,1-*b*][1,3,4]thiadiazole-5-carbaldehydes. The absence of aldehyde protons and presence of the methylidene proton around δ 7.7 in ^{1}H NMR spectra of the product supported the formation of title compounds (**6a-g**) and (**7a-g**).

3.2. Antimicrobial activity

The fourteen synthesized compounds were screened for their antibacterial and antifungal screening using twofold serial dilution technique [32].

All compounds were tested against two Gram-negative (*Escherichia coli* (ATCC 35218), *Pseudomonas aeruginosa* (ATCC 25619)) and two Gram-positive (*Staphylococcus aureus* (ATCC 25923), *Enterococcus faecalis* (ATCC 35550)) bacterial strains. All the synthesized compounds exhibited varying degree of inhibitory effect on the growth of different tested strains Table 1. Compounds **6e**, **6f**, **7e** and **7f** showed significant activity against *S. aureus* and *E. faecalis* and moderate against *E. coli, P.aeruginosa*, suggesting that the substitution of 4-bromopheny and 4-chlorophenyl groups might contribute to their increased activities while 4-methylphenyl, 4-methoxylphenyl and 4-nitrophenyl groups at 6th position of imidazo[2,1-*b*][1,3,4] thiadiazole might not be preferable. Whereas, compounds **6a**, **6b**, **6c**, **6d**, **6g**, **7a**,**7b**, **7c**,**7d** and **7g** showed weak to moderate activity.

The antifungal screening of all compounds was carried against four fungal strains, *Candida albicans* (ATCC 2091), *Aspergillus flavus* (NCIM No. 524), *Aspergillus niger* (ATCC 6275), and *Cryptococcus neoformans* (clinical isolate). All synthesized compounds showed significant antifungal activity against different fungal strains. Although compounds **7e** and **7f** showed good antifungal activity against all the fungal strains, compounds **6e** and **6f** also showed remarkable activity against all the fungal strains. All other compounds showed moderate activity against all the fungal strains but compounds **6a**, **6b**, **6d** showed weak activity against *A. niger* and **6b** against *A. flavus*.

A total analysis of the antibacterial and antifungal activity revealed that (*i*) the 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) acetic acids are shown good activity as compare 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo [2,1-b][1,3,4] thiadiazol-5-yl)methylene)-2,4-dioxothiazolidin-3-yl) acetic acids; (*ii*) The antibacterial and antifungal activity imidazo [2,1-*b*][1,3,4]thiadiazole derivatives depended upon the presence and nature of the substituents, which were introduced into the imidazo[2,1-*b*][1,3,4]thiadiazole ring. (*iii*) The antibacterial and antifungal activity of imidazo[2,1-*b*] [1,3,4]thiadiazole derivatives were enhanced by the introduction of electron withdrawing 4-bromophenyl and 4-chlorophenyl group 6th position of imidazo[2,1-*b*][1,3,4] thiadiazole.

4. Conclusion

We have synthesized several 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-b][1,3,4]thiadiazol-5-yl) methylene)-2,4-dioxothiazolidin-3-yl) acetic acid and 2-((5*Z*)-5-((2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-b][1,3,4] thiadiazol-5-yl)methylene)-4-oxo-2-thioxothiazolidin-3-yl) acetic acid derivatives. The results of the in-vitro antimicrobial activity are also encouraging as out of 14 compounds tested, compounds **6e**, **6f**, **7e** and **7f** exhibited antimicrobial activity. A total analysis of the antibacterial and antifungal activity revealed that the antibacterial and antifungal activity of imidazo[2,1-*b*][1,3,4]thiadiazole derivatives were enhanced by the introduction of 4-bromopheny and 4-chlorophenyl group 6th position of imidazo[2,1-*b*][1,3,4]thiadiazole and the mode of action of these compounds was unknown. These observation may promote a further development of this group of imidazo[2,1-*b*][1,3,4]thiadiazoles and may lead to compounds with better pharmacological profile then standard antibacterial and antifungal drugs.

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