Synthesis and in Vitro Antimicrobial Evaluation of Benzothiazole Incorporated Thiazolidin-4-ones Derivatives

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ABSTRACT. In the course of work on new pharmacologically active antimicrobial agents, we have reported the synthesis of a new class of structurally novel derivatives, incorporating two bioactive structures, a benzothiazole and thiazolidin-4-one, to yield a class of compounds having interesting antimicrobial properties. The antimicrobial properties of the synthesized compounds were investigated against bacteria (Staphylococcus aureus and Escherchia coli) and fungi (Candida albicans and Aspergillus niger) using serial plate dilution method. The structure of the synthesized compounds have been established by elemental analysis and spectroscopic data. 

Key words: Benzothiazole, Thiazolidin-4-ones, N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine carboxamide, Antimicrobial activity

INTRODUCTION

Nitrogen heterocycles are the basis of many essential pharmaceuticals and of many physiologically active natural products. Despite the numerous attempts to develop new structural prototype in the search for effective antimicrobials, benzothiazole still remain as one of the most versatile class of compounds against microbes and therefore, are useful substructures for further molecular exploration. Benzothiazole derivatives have attracted continuing interest because of their varied biological activities viz. antitubercular,1,2 antihelminthic,3 anti-inflammatory,2 antimicrobial,5,6 and antiviral.7 Thiazolidin-4-one derivatives are known to exhibit diverse biological activities such as anticonvulsant,15,16 antihistaminic,17,18 and antioxidant.19 In continuation of our interest in the synthesis of heterocycles containing benzothiazole moiety, to identify new candidates that may be of value in designing new, potent, selective, and less toxic antimicrobial agents, we report here the synthesis and antimicrobial evaluation of some novel structural hybrids incorporating the benzothiazole moiety with thiazolidin-4-one ring systems through different linkages. This combination was taken in an attempt to investigate the influence of such hybridization and structural variation on the anticipated antimicrobial activity, hoping to add some synergistic biological importance to the target molecules. The substitution pattern of thiazolidin-4-one rings was carefully chosen so as to confer varied electronic environment to the molecules.

EXPERIMENTAL

Melting points (m.p.) of the synthesized compounds were determined in open capillary tubes and were uncorrected. All the compounds were subjected to elemental analysis (CHN) by Perkin Elmer 2400 CHN analyzer and the measured values agreed within ±0.4% with the calculated ones. The IR spectra were recorded in KBr pellets on SCHIMADZU 8400 S FTIR spectrophotometer. 1H NMR and 13C NMR spectra were obtained from JEOL AL 300 FT NMR using TMS as internal standard in CDCl3/DMSO-d6. The mass spectra were recorded on JEOL SX 102/DA600 using Argon/Xenon as FAB gas. The purity of synthesized compounds were checked by TLC using Silica gel “G” as adsorbent and visualization was accomplished by UV light or iodine.

Synthesis of 3,5-Dimethylphenylthiourea 2

3,5-dimethylaniline 1 (0.1 mol), hydrochloric acid (9 ml), and water (25 ml) were taken and refluxed for 30 min in a round bottomed flask. The contents were cooled down to room temperature and then ammonium thiocyanate (0.1 mol) was added. The reaction mixture was again refluxed for 4 h. The solid obtained was cooled down, filtered,
washed well with water, dried, and crystallized from ethanol.

**Synthesis of 2-Amino-5,7-dimethylbenzothiazole 3**

In a round-bottomed flask equipped with a mechanical stirrer and a dropping funnel, 5,7-dimethyl phenylthiourea 2 (0.1 mol) and chloroform (100 ml) were taken. A solution of bromine (0.1 mol) in chloroform (100 ml) was added dropwise with stirring for a period of two hours. Temperature of reaction mixture remains below 5 °C during the reaction. Stirring was continued for a period of 4 h. After the addition of bromine solution, the contents of round-bottomed flask were refluxed for about 4 h till the contents of the mixture became turbid and the volume reduced to half of the original. The contents were further added to ice water. The solid obtained was filtered off, dried and recrystallized from a suitable solvent. White solid; Yield: 68%; m.p. 157 °C.

A mixture of compound 4 and hydrazine hydrate (1:1 mol) was dissolved in methanol at room temperature. To the solution, conc. NaOH was added and refluxed for 6 h. The reaction mixture was poured into crushed ice and recrystallized from a suitable solvent. Light solid; Yield: 85%; m.p. 141 °C.

**Synthesis of 1-(5,7-Dimethylbenzo[d]thiazol-2-yl)urea 4**

To the solution of sodium cyanate, dissolved in minimum quantity of water, glacial acetic acid (5 ml) was added. An alcoholic solution of 2-amino-5,7-dimethylbenzothiazole 3 was added and the solution was heated till the contents of the mixture became turbid and the volume reduced to half of the original. The contents were further added to ice cool water. The solid obtained was filtered off, dried and recrystallized from ethan-ol.

**Synthesis of N-(5,7-Dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 5**

A mixture of compound 4 and hydrazine hydrate (1:1 mol) was dissolved in methanol at room temperature. To the solution, conc. NaOH was added and refluxed for 6 h. Few drops of glacial acetic acid was added to the reaction mixture and was then refluxed on a water bath for 5–6 h and was then allowed to cool, poured onto crushed ice and recrystallized from methanol.

**Synthesis of 2-Substituted Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6a–h**

An equimolar mixture of 5 (0.1 mol) and substituted benzaldehyde (0.1 mol) was dissolved in methanol at room temperature. Few drops of glacial acetic acid was added to the reaction mixture and was then refluxed on a water bath for 5–6 h and was then allowed to cool, poured onto crushed ice and recrystallized from methanol.

A mixture of compound 4 and hydrazine hydrate (1:1 mol) was dissolved in methanol at room temperature. To the solution, conc. NaOH was added and refluxed for 6 h. The reaction mixture was poured into crushed ice and recrystallized from a suitable solvent. Light solid; Yield: 85%; m.p. 141 °C.

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6a**

Yellow solid; Yield: 74%; m.p. 151 °C; Anal. calcd. for C_{17}H_{18}N_{2}O: C, 56.90; H, 4.18; N, 15.62%. Found: C, 56.99; H, 4.25; N, 15.75%; IR (KBr) (ν_{max}/cm^{-1}): 3318 (NH), 1675 (C=O), 1585 (C=N), 665 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 7.35 (1H, s, N=CH); MS, m/z (%) 324 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6b**

White solid; Yield: 70%; m.p. 172 °C; Anal. calcd. for C_{17}H_{18}ClN_{2}O: C, 53.55; H, 3.66; N, 14.28%. Found: C, 51.98; H, 3.65; N, 14.34%; IR (KBr) (ν_{max}/cm^{-1}): 3320 (NH), 1665 (C=O), 1582 (C=N), 661 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.16 (1H, s, N=CH); MS, m/z (%) 393 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6c**

White solid; Yield: 70%; m.p. 172 °C; Anal. calcd. for C_{17}H_{18}ClN_{2}O: C, 53.55; H, 3.66; N, 14.28%. Found: C, 51.98; H, 3.65; N, 14.34%; IR (KBr) (ν_{max}/cm^{-1}): 3320 (NH), 1665 (C=O), 1582 (C=N), 661 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.16 (1H, s, N=CH); MS, m/z (%) 393 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6d**

White solid; Yield: 85%; m.p. 141 °C; Anal. calcd. for C_{17}H_{18}ClN_{2}O: C, 53.55; H, 3.66; N, 14.28%. Found: C, 51.98; H, 3.65; N, 14.34%; IR (KBr) (ν_{max}/cm^{-1}): 3320 (NH), 1665 (C=O), 1582 (C=N), 661 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.16 (1H, s, N=CH); MS, m/z (%) 393 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6e**

Light brown solid; Yield: 65%; m.p. 145 °C; Anal. calcd. for C_{17}H_{18}N_{2}O: C, 63.75; H, 5.44; N, 16.70%. Found: C, 63.75; H, 5.44; N, 16.70%; IR (KBr) (ν_{max}/cm^{-1}): 3310 (NH), 1668 (C=O), 1585 (C=N), 645 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.12 (1H, s, N=CH); MS, m/z (%) 338 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6f**

White solid; Yield: 85%; m.p. 141 °C; Anal. calcd. for C_{17}H_{18}ClN_{2}O: C, 53.55; H, 3.66; N, 14.28%. Found: C, 51.98; H, 3.65; N, 14.34%; IR (KBr) (ν_{max}/cm^{-1}): 3320 (NH), 1665 (C=O), 1582 (C=N), 661 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.16 (1H, s, N=CH); MS, m/z (%) 393 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6g**

Light brown solid; Yield: 65%; m.p. 145 °C; Anal. calcd. for C_{17}H_{18}N_{2}O: C, 63.75; H, 5.44; N, 16.70%. Found: C, 63.75; H, 5.44; N, 16.70%; IR (KBr) (ν_{max}/cm^{-1}): 3310 (NH), 1668 (C=O), 1585 (C=N), 645 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.12 (1H, s, N=CH); MS, m/z (%) 338 (M^{+}).

**Synthesis of 2-Benzimididene-N-(5,7-dimethylbenzo[d]thiazol-2-yl)hydrazine Carboxamide 6h**

White solid; Yield: 85%; m.p. 141 °C; Anal. calcd. for C_{17}H_{18}ClN_{2}O: C, 53.55; H, 3.66; N, 14.28%. Found: C, 51.98; H, 3.65; N, 14.34%; IR (KBr) (ν_{max}/cm^{-1}): 3320 (NH), 1665 (C=O), 1582 (C=N), 661 (C=S–C benzothiazole); 1H NMR (300 MHz, DMSO-d_{6}, δ/ppm): 9.16 (1H, s, N=CH); MS, m/z (%) 393 (M^{+}).
Synthesis of 1-(5,7-Dimethylbenzo[d]thiazol-2-yl)-3-(2-(2-chlorophenyl)-4-oxo-thiazolidin-3-yl)urea 7b

Yellow solid; Yield: 75%; m.p. 238 °C; Anal. Caled. for C_{19}H_{12}ClN_{2}O_{2}S: C, 52.71; H, 3.93; N, 12.94%. Found: C, 52.82; H, 3.76; N, 13.03%. IR (KBr) (ν_max/cm⁻¹): 3208 (NH), 3120 (C==H aromatic), 1720 (C==O thiazolidinone), 1666 (C==O), 1545 (C==C aromatic), 1440 (C==N benzothiazole), 695 (C==S thiazolidinone), 619 (C==S benzothiazole); ²⁷NMR (300 MHz, DMSO-d₆, δ/ppm): 174.5, 168.9, 154.3, 147.9, 129.8, 134.2, 127.2, 131.8, 120.3, 138.7, 134.2, 128.9, 128.2, 126.5, 130.3, 48.8, 37.5 (CH₂ thiazolidinone), 21.2, 17.6; MS, m/z (%) 432.5 (M⁺).

Synthesis of 1-(5,7-Dimethylbenzo[d]thiazol-2-yl)-3-(2-(2-dichlorophenyl)-4-oxo-thiazolidin-3-yl)urea 7c

Light brown solid; Yield: 68%; m.p. 212 °C; Anal. Caled. for C_{20}H_{12}Cl₂N_{2}O_{2}S: C, 58.25; H, 3.42; N, 11.99%. Found: C, 58.41; H, 3.55; N, 12.12%. IR (KBr) (ν_max/cm⁻¹): 3215 (NH), 3110 (C==H aromatic), 1732 (C==O thiazolidinone), 1660 (C==O), 1530 (C==C aromatic), 1425 (C==N benzothiazole), 678 (C==S thiazolidinone), 610 (C==S benzothiazole); ²⁷NMR (300 MHz, DMSO-d₆, δ/ppm): 11.85 (1H, s, CONH), 8.02 (1H, s, NH), 7.62–7.80 (6H, m, Ar–H), 2.45 (2H, s, CH₂ thiazolidinone); ¹³C NMR (300 MHz, DMSO-d₆, δ/ppm): 174.5, 168.9, 154.0, 149.2, 129.0, 134.5, 127.0, 131.2, 129.5, 136.8, 135.6, 129.2, 133.6, 126.5, 130.2, 48.7, 37.2 (CH₂ thiazolidinone), 20.2, 15.6; MS, m/z (%) 467 (M⁺).
14.5; MS, m/z (%) 412 (M⁺).

1-(5,7-Dimethylenbenzod[thiazol-2-yl]-3-(2-(2-methoxyphenyl)-4-oxo-thiazolidin-3-yl)urea 7g

White solid; Yield: 59%; m.p. 278 °C; Anal. Calcld. for C₃₂H₂₄N₂O₆S₂: C, 56.07; H, 4.67; N, 13.08%. Found: C, 56.17; H, 4.78; N, 13.01%; IR (KBr) (νmax/cm⁻¹): 3232 (NH), 3120 (C–H aromatic), 1722 (C=O thiazolidinone), 1672 (C=O), 1545 (C=C aromatic), 1433 (C–N benzothiazole), 1380 (C–S benzothiazole); ¹H NMR (300 MHz, DMSO-d₆, δ/ppm): 11.80 (1H, s, CONH), 8.05 (1H, s, NH), 7.65–7.72 (6H, m, Ar–H), 2.53 (2H, s, CH₂ thiazolidinone), 3.85 (1H, s, OCH₃), 1.56, 56.3 (OCH₃); MS, m/z (%) 428 (M⁺).

1-(5,7-Dimethylenbenzod[thiazol-2-yl]-3-(2-(4-nitrophenyl)-4-oxo-thiazolidin-3-yl)urea 7f

White solid; Yield: 68%; m.p. 203 °C; Anal. Calcld. for C₃₂H₂₂N₂O₅S₂: C, 51.46; H, 3.83; N, 15.80%. Found: C, 51.35; H, 3.92; N, 15.89%; IR (KBr) (νmax/cm⁻¹): 3235 (NH), 3140 (C–H aromatic), 1739 (C=O thiazolidinone), 1690 (C=O), 1554 (C=C aromatic), 1460 (C–N benzothiazole), 690 (C–S–C benzothiazole), 608 (C–S–C benzothiazole); ¹H NMR (300 MHz, DMSO-d₆, δ/ppm): 11.62 (1H, s, CONH), 8.10 (1H, s, NH), 7.52–7.59 (6H, m, Ar–H), 2.56 (2H, s, CH₂ thiazolidinone); ¹³C NMR (300 MHz, DMSO-d₆, δ/ppm): 174.5, 168.8, 153.8, 148.2, 129.0, 134.1, 134.2, 129.8, 128.5, 127.3, 126.9, 131.8, 129.2, 128.5, 124.8, 38.5 (CH₃ thiazolidinone), 20.5, 15.0; MS, m/z (%) 443 (M⁺).

1-(5,7-Dimethylenbenzod[thiazol-2-yl]-3-(2-(2-hydroxyphenyl)-4-oxo-thiazolidin-3-yl)urea 7h

White yellow solid; Yield: 52%; m.p. 215 °C; Anal. Calcld. for C₃₄H₂₅N₂O₅S₂: C, 54.16; H, 3.83; N, 15.80%. Found: C, 54.21; H, 3.43; N, 15.41%; IR (KBr) (νmax/cm⁻¹): 3231 (NH), 3135 (C–H aromatic), 1736 (C=O thiazolidinone), 1687 (C=O), 1548 (C=C aromatic), 1447 (C–N benzothiazole), 696 (C–S–C thiazolidine), 617 (C–S–C benzothiazole); ¹H NMR (300 MHz, DMSO-d₆, δ/ppm): 11.68 (1H, s, CONH), 8.02 (1H, s, NH), 7.45–7.51 (6H, m, Ar–H), 2.48 (2H, s, CH₂ thiazolidinone); ¹³C NMR (300 MHz, DMSO-d₆, δ/ppm): 174.5, 168.5, 154.3, 149.0, 129.2, 134.5, 127.2, 131.5, 128.5, 141.5, 132.5, 131.0, 129.1, 127.4, 131.6, 49.2, 35.6 (CH₂ thiazolidinone), 20.5, 15.2; MS, m/z (%) 414 (M⁺).

1-(5,7-Dimethylenbenzod[thiazol-2-yl]-3-(2-(2-bromophenyl)-4-oxo-thiazolidin-3-yl)urea 7e

Brownish yellow solid; Yield: 62%; m.p. 220 °C; Anal. calcld. for C₃₄H₂₂BrN₂O₅S₂: C, 47.79; H, 3.56; N, 11.74%; IR (KBr) (νmax/cm⁻¹): 3242 (NH), 3125 (C–H aromatic), 1729 (C=O thiazolidinone), 1688 (C=O), 1552 (C=C aromatic), 1442 (C–N benzothiazole), 698 (C–S–C thiazolidine), 620 (C–S–C benzothiazole); ¹H NMR (300 MHz, DMSO-d₆, δ/ppm): 11.62 (1H, s, CONH), 8.11 (1H, s, NH), 7.44–7.55 (6H, m, Ar–H), 2.53 (2H, s, CH₂ thiazolidinone); ¹³C NMR (300 MHz, DMSO-d₆, δ/ppm): 174.5, 168.9, 153.0, 148.2, 129.0, 134.5, 129.0, 130.6, 129.2, 157.6, 120.5, 131.8, 129.1, 130.2, 129.2, 52.3, 39.2 (CH₂ thiazolidinone), 21.2, 15.9; MS, m/z (%) 477 (M⁺).

**BIOLICAL STUDY**

The synthesized compounds 7a–h were tested for their in vitro antimicrobial activity against the Gram positive bacteria *Staphylococcus aureus* and the Gram negative bacteria *Escherichia coli* in nutrient agar media and fungi (*Candida albicans* and *Aspergillus niger*) in Sabouraud dextrose medium at 200, 100, 50, 25 and 12.5 µg/mL⁻¹ by using serial plate dilution method in DMSO. Standard antibiotics ofloxacin and ketoconazole were used as reference drugs at 50, 25 and 12.5 µg/mL⁻¹ concentrations. The MIC’S (minimum inhibitory concentration) values were determined by comparison to ofloxacin and ketoconazole as the standard drugs for bacterial and fungial activity respectively.

**RESULTS AND DISCUSSION**

The synthesis of compounds 6a–h was accomplished by reacting N-(5,7-dimethylenbenzod[thiazol-2-yl]hydrazine carboxamide 5 with substituted aromatic aldehydes in ethanol. The salt 6a–h underwent ring closure via condensation with thioglycollic acid to give 1-(5,7-dimethyl benzo[d]thiazol-2-yl)-3-(4-oxo-substituted phenyl thiazolidin-3-yl) urea 7a–h. The synthetic pathway followed for the synthesis of the title compounds is described in Scheme 1.

The structure of the synthesized compounds was confirmed by elemental analysis and spectral data (IR, ¹H NMR, ¹³C NMR and MS spectroscopy). The IR spectra of compounds 6a–h showed absorption peaks at 3310–3320 and 1660–1675 cm⁻¹ due to N–H and C=O stretching vibrations. The appearance of the stretching of the C=O of thiazolidine at 1720–1739 cm⁻¹ in the spectra of derivatives together with the C=O stretching at 1660–1690 cm⁻¹ confirmed the formation of the compounds 7a–h.

The ¹H-NMR spectra of compounds 6a–h showed a multiplet at δ 7.75–7.90 ppm for the aromatic ring and singlets at δ 6.25 and 7.98 ppm for –NH and –N=CH respectively.

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The disappearance of the singlet peak of –N=CH and the presence of a singlet peak at δ 2.46 ppm of –CH$_2$ of thiazolidinone proved that these compounds participated in the cyclization reaction and formed the desired compounds 7a−h. This was further confirmed by $^{13}$C NMR of the synthesized compounds 7a−h which showed peaks at δ 35.6−39.2 ppm conforming the presence of –CH$_2$ of thiazolidine ring. The elemental analysis and molecular ion peak of compounds 7a−h were consistent with the assigned structures.

**ANTIMICROBIAL ACTIVITY**

The synthesized compounds were tested for their antibacterial and antifungal activity using serial plate dilution method. The compounds showed good to moderate inhibition at 12.5−200 µg/mL in DMSO. The compounds 7b, 7c, 7f and 7h showed comparatively good activity against all bacterial strains. The good activity is attributed to the presence of biologically active 2-chloro (7b), 2,4-dichloro (7c), 4-nitro (7f) and 2-bromo (7h) groups attached to the phenyl group at position 2 of the thiazolidin-4-one ring. Compounds 7a, 7e and 7g exhibited moderate activity compared to that of ofloxacin against all the bacterial strains (Table 1).

Compounds 7b, 7c and 7f showed good activity against all the fungal strains. The structure of these compounds contain biologically active 2-chloro (7b), 2,4-dichloro (7c) and 4-nitro (7f) and groups attached to the phenyl group at position 2 of the thiazolidin-4-one ring. Compounds 7a and 7h showed moderate activity compared to that of ketoconazole against all the fungal strains (Table 2).

**CONCLUSION**

The newly synthesized compounds 7a−h presented here differ in their corresponding antimicrobial activity depending upon the type of substituent in hybrid molecules. The presence of 2,4-dichloro, 2-chloro, 4-nitro and 2-bromo groups attached to the phenyl group at position 2 of the thiazolidin-4-ones ring showed good activity against all the bacterial strains. The presence of 2,4-dichloro, 2-chloro and 4-nitro groups attached to the phenyl group at posi-

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**Table 1. Antibacterial activity of the synthesized compounds (7a−h)**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Zone of inhibition in mm and MIC in µg/mL</th>
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<tbody>
<tr>
<td></td>
<td><em>S.aureus</em></td>
</tr>
<tr>
<td>7a</td>
<td>14(100)</td>
</tr>
<tr>
<td>7b</td>
<td>22(25)</td>
</tr>
<tr>
<td>7c</td>
<td>22(25)</td>
</tr>
<tr>
<td>7d</td>
<td>7(&lt;200)</td>
</tr>
<tr>
<td>7e</td>
<td>15(100)</td>
</tr>
<tr>
<td>7f</td>
<td>27(12.5)</td>
</tr>
<tr>
<td>7g</td>
<td>12(100)</td>
</tr>
<tr>
<td>7h</td>
<td>24(25)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>22(25)</td>
</tr>
</tbody>
</table>

The figures in the table show the zone of inhibition (mm) and the corresponding MIC (µg/mL) values in brackets.

**Table 2. Antifungal activity of the synthesized compounds (7a−h)**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Zone of inhibition in mm and MIC in µg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>C.albicans</em></td>
</tr>
<tr>
<td>7a</td>
<td>18(50)</td>
</tr>
<tr>
<td>7b</td>
<td>30(12.5)</td>
</tr>
<tr>
<td>7c</td>
<td>29(12.5)</td>
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<tr>
<td>7d</td>
<td>19(50)</td>
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<tr>
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<td>20(50)</td>
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<tr>
<td>7f</td>
<td>29(12.5)</td>
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<tr>
<td>7g</td>
<td>19(50)</td>
</tr>
<tr>
<td>7h</td>
<td>22(25)</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>30(12.5)</td>
</tr>
</tbody>
</table>

The figures in the table show the zone of inhibition (mm) and the corresponding MIC (µg/mL) values in brackets.

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Scheme 1. Reaction scheme for synthesis of compounds 7a−h.
tion 2 of the thiazolidin-4-one ring showed good activity against all the fungal strains. The result also showed that gram negative showed better activity than gram positive organisms. Thus, heterocycles accommodating sub units i.e. benzothiazole and thiazolidin-4-one are expected to prove the therapeutic relevance and their utility in medicinal chemistry. Our ongoing research focuses on the same molecular hybrids with incorporation of more effective substituents in search of new effective antimicrobial agents.

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