Synthesis of new derivatives of N-(1H-indol-5-yl)-2-(((5-
substituted benzo[d]thiazol-2-yl)methyl)amino)acetamides and
their antimicrobial activity

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Abstract: A number of new derivatives of N-(1H-indol-5-yl)-2-(((5-
substituted benzol[d]thiazol-2-yl)methyl)amino)acetamides (6a-n) are prepared by the reaction of (5-
substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n) with 2-chloro-N-(1H-indol-5-yl)acetamide (3) in presence of sodium methoxide in DMF. The antibacterial and antifungal activity of all the new derivatives of N-(1H-indol-5-yl)-2-(((5-
substituted benzol[d]thiazol-2-yl)methyl)amino)acetamides (6a-n) were evaluated against some bacterial and fungal strains and showed promising results. The structures of the resulted compounds were identified and confirmed by elemental analysis, mass, ¹HNMR and ¹³CNMR spectroscopies.

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I. Introduction

Benzothiazoles are heterocyclic compounds in which thiazole ring is fused with benzene ring. These are part of compounds showing numerous biological activities such as antimicrobial,¹-⁵ anticancer,⁶-⁹ anthelmintic,¹⁰ and anti-diabetic¹¹ activities. They have also found application in industry as antioxidants, vulcanization accelerators. Various benzothiazoles such as 2-aryl benzothiazole received much attention due to the unique structure and its uses as radioactive amyloid imagining agents¹² and anticancer agents.¹³ The compound (S)-2,6-diamino-N-(4-(5-
fluorobenzo[d]thiazol-2-yl)-2-methylphenyl)hexanamide was found to possess potent antitumor activity.¹⁴-¹⁵

3-(4-(5-chlorobenzo[d]thiazol-2-yl)-1-phenyl-1H-pyrazol-3-yl)phenyl acetate shows significant antitumor activity against both gram positive and gram negative bacteria.

N-(3-mercapto-5-(pyridin-3-yl)-4H-1,2,4-triazol-4-yl)benzo[d]thiazole-2-carboxamide show significant antibacterial and antifungal activity.¹⁷,¹⁸
Synthesis of new derivatives of N-(1H-indol-5-yl)-2-(((5-substituted benzo[d]thiazol-2-..)

2-amino[5′(4-sulphonylbenzylidine)-2, 4-thiazolidinone]-7-chloro-6-flouro benzothiazoles were showed promising anti-diabetic activity.19

Where R= H, m-NO2, p-COOH, , , ,

An indole is characterized as a benzene ring fused with nitrogen containing five membered heterocyclic rings. Indoles are of interest in many pharmaceutical areas, since they exhibit a variety of biological properties20-23. A number of C-3, C-5-substituted indoles were synthesized and studied for their biological affinities24.

Indole sulfonamide derivatives of type (cyclopentyl (3-(2-methoxy-4-((o-tolylsulfonyl)carbamoyl)benzyl)-1-methyl-1H-indol-5-yl)carbamate) act as human Anti-asthamatic25, (1-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide) for the treatment of migraine and cluster headaches and (5-(4-(4-(5-cyano-1H-indol-3-yl)butyl)piperazin-1-yl)benzofuran-2-carboxamide) act as antidepressant.

(cyclopentyl (3-(2-methoxy-4-((o-tolylsulfonyl)carbamoyl)benzyl)-1-methyl-1H-indol-5-yl)carbamate)

(1-(3-(2-(dimethylamino)ethyl)-1H-indol-5-yl)-N-methylmethanesulfonamide)
Synthesis of new derivatives of N-(1H-indol-5-yl)-2-((5-substituted benzo[d]thiazol-2-yl)methyl)amino)acetamides. All the synthesized compounds were screened for their antimicrobial activity.

**II. Results And Discussion**

**Synthesis:** New derivatives of N-(1H-indol-5-yl)-2-((5-substituted benzo[d]thiazol-2-yl)methyl)amino)acetamides (6a-n) are synthesized from the reaction of (5-substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n) with 2-chloro-N-(1H-indol-5-yl)acetamide (3) in presence of sodium methoxide in DMF. The compound 2-chloro-N-(1H-indol-5-yl)acetamide (3) is prepared from the reaction of 1H-indol-5-amine (1) with 2-chloroacetyl chloride(2) in presence of sodium acetate and acetic acid in water. The compounds of (5-substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n) are synthesized from 2-amino-4-substitutedbenzenethiols (1a-n) with 2-hydroxyacetic acid (2a) in presence of conc. hydrochloric acid at 100°C yields (5-substitutedbenzo[d]thiazol-2-yl)methanol(3a-n). The reaction of (5-substitutedbenzo[d]thiazol-2-yl)methanol(3a-n) with Phthalimide impresence of PPh₃, DEAD in THF followed by with hydradine hydrate in ethanol produces (5-substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n). The structures final derivatives were confirmed by IR, ¹HNMR, ¹³CNMR and Mass spectral analysis.

**Scheme:**

1H-indol-5-amine (1) + 2-Chloroacetyl chloride (2) → 2-Chloro-N-(1H-indol-5-yl)acetamide (3) + Sodium acetate / water + Acetic acid

1H-indol-5-amine (1) + 2-Hydroxyacetic acid (2a) → (5-Substitutedbenzo[d]thiazol-2-yl)methanols (3a-n) + Conc. HCl / 100°C

(5-Substitutedbenzo[d]thiazol-2-yl)methanols (3a-n) + Phthalimide (4) → (5-Substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n) + NH₂NH₂H₂O / EtOH

(5-Substitutedbenzo[d]thiazol-2-yl)methanamines (5a-n) + NaOMe / DMF → 2-((5-Substitutedbenzo[d]thiazol-2-yl)methylamino)-N-(1H-indol-5-yl)acetamides (6a-n)
Synthesis of new derivatives of N-(1H-indol-5-yl)-2-((5-substituted benzo[d]thiazol-2-yl)ethyl)benzaldehyde.

Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
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<tbody>
<tr>
<td>6a</td>
<td>H</td>
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<tr>
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<td>BnO</td>
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<tr>
<td>6d</td>
<td>i-PrO</td>
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<tr>
<td>6e</td>
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<tr>
<td>6f</td>
<td>(3,4-C2C6H5CH2O)-</td>
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<tr>
<td>6h</td>
<td>CF3HClO</td>
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<tr>
<td>6i</td>
<td>CN</td>
</tr>
<tr>
<td>6j</td>
<td>Me</td>
</tr>
<tr>
<td>6k</td>
<td>C2H5</td>
</tr>
<tr>
<td>6l</td>
<td>F</td>
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</tr>
<tr>
<td>6n</td>
<td>Br</td>
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</tbody>
</table>

Antibacterial activity: The antibacterial activity of was carried out by testing all the synthesized compounds against Escherichia coli, Pseudomonas, Serratia and bacillus cereus.

Almost all the compounds showed promising activity that could be attributed to the presence of thiazole and indole heterocyclic ring systems with their high potency. The compound 6a, 6b, 6c, 6e, 6d, 6h, 6j and 6k shows high activity with all strains of bacteria. The compounds 6l, 6m and 6n are highly active against Escherichia coli and Pseudomonas. The remaining compounds were showed moderately active against all strains.

Table no 2

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<th>S.No</th>
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<th>P.aeruginosa</th>
<th>E.coli</th>
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Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = + + (inhibition zone 10-13 mm); highly active = + + + (inhibition zone > 14 mm).

Antifungal activity. The antifungal activity of the synthesized compounds 6a-n against Aspergillous niger and Candida albicans, using fluconazole as standard (Table 3). Compounds 6k, 6l, 6m and 6n were showed highly active. The remaining compounds were slightly to moderately active against both strains.

Table no 3. Antifungal activity of the test compounds 6a-n

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound</th>
<th>Aspergillus niger</th>
<th>Candida albicans</th>
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<tbody>
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<td>10(++)</td>
</tr>
<tr>
<td>2</td>
<td>6b</td>
<td>12(++)</td>
<td>12(++)</td>
</tr>
<tr>
<td>3</td>
<td>6c</td>
<td>11(++)</td>
<td>10(++)</td>
</tr>
<tr>
<td>4</td>
<td>6d</td>
<td>07(+)</td>
<td>08(+)</td>
</tr>
<tr>
<td>5</td>
<td>6e</td>
<td>08(+)</td>
<td>10(++)</td>
</tr>
<tr>
<td>6</td>
<td>6f</td>
<td>07(+)</td>
<td>09(+)</td>
</tr>
<tr>
<td>7</td>
<td>6g</td>
<td>09(+)</td>
<td>09(+)</td>
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<tr>
<td>8</td>
<td>6h</td>
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<td>11(++)</td>
</tr>
<tr>
<td>9</td>
<td>6i</td>
<td>12(++)</td>
<td>10(++)</td>
</tr>
<tr>
<td>10</td>
<td>6j</td>
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</tr>
<tr>
<td>11</td>
<td>6k</td>
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<td>19(++)</td>
</tr>
<tr>
<td>12</td>
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<td>16(+)</td>
</tr>
<tr>
<td>13</td>
<td>6m</td>
<td>19(+)</td>
<td>18(+)</td>
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<td>15</td>
<td>Fluconazole</td>
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</tr>
</tbody>
</table>
Key to symbols: - inactive (inhibition zone < 6 mm); slightly active = + (inhibition zone 7–9 mm); moderately active = ++ (inhibition zone 10-13 mm); highly active = +++ (inhibition zone > 14 mm).

### III. Experimenta procedure

All the melting points are uncorrected. The purity was checked by thin layer chromatography with silica gel 60 GF254 E.Merck precoated plates (0.25 mm) was visualized using UV. 0.1 for flash chromatography on silica gel (particle size 100-200 mesh). and characterized by spectral studies. The IR spectra were recorded on shimadzu FTIR model 8010 spectrophotometer and are given in cm\(^{-1}\) in KBr. The \(^1\)HNMR & \(^{13}\)CNMR spectra were recorded on Bruker AM-400 NMR spectrometers in deuterated chloroform and deuterated DMSO. The chemical shifts are reported in \(\delta\) (ppm) relative to tetramethylsilane as internal standard. Mass spectra analyses performed with an Agilent 6400 Series equipped with an electro spray ionization source (capillary voltage at 4000V, nebulizing gas temperature at 300 °C, nebulizing gas flow at 12 L/ min).

#### General Procedure for the preparation of \((5\text{-substituted-benzo}[d]\text{thiazol-2-yl})\text{methanol (3a-n)}:

To a mixture of 2-amino-4-substitutedbenzenethiol (5gm) and glycolic acid(3 m.eq.) was added HCl (4 N, 30vol). The reaction was allowed to proceed with refluxing at 100 °C for 6-8 hrs, prior to being quenched with saturated aqueous sodium bicarbonate. The solution was extracted with ethyl acetate (20 vol × 3). The combined extracts was evaporated in vacuo to give the crude product, which was subjected to the coloumn chromatography using DCM/MeOH (100/2, v/v) as eluent to yield the title compound (5-substituted-benzo[d]thiazol-2-yl)methanol in 15-30% yield.

**General Procedure for the preparation of \((5\text{-substituted-benzo}[d]\text{thiazol-2-yl})\text{methanamines (5a-n)}:**

To a solution of (5-substituted-benzo[d]thiazol-2-yl)methanol (1 gm) in THF (45 ml) was added triphenylphosphine(2.0 m.eq), phthalimide (2.0 m.eq) and diethyl azodicarboxylate (2.0 m.eq) and stirred at room temperature for 2 more days, then it was cooled in ice-bath. The mixture was diluted with water and ethylacetate, then extracted with ethylacetate, washed with brine, dried over MgSO\(_4\) and concentrated under reduced pressure. The mixture was stirred at room temperature for overnight, then it was added ammonium chloride (13.0 m.eq). The mixture was stirred at room temperature for 2 more days, then it was cooled in ice-bath, added HCl/EtOAc, and stirred for 2-6 h more without ice-bath. The mixture was concentrated under reduced pressure, and the resulting solid was dissolved to Hexane/EtOAc = 1/1 (15vol), stirred at room temperature for 20-60 min, then it was filtered to obtain the title compound.

**Compound-5a: benzo[d]thiazol-2-ylmethanamine:**

Yield :47 %, M.P. : 125-127°C, IR (KBr): 3380 cm\(^{-1}\)(-NH\(_2\)), 3050cm\(^{-1}\)(=C-H), 1590(-C=N), \(^1\)H-NMR(DMSO-d\(_6\)) : \(\delta\) 4.40(2H, s, -CH\(_2\)), 5.18 (2H, bs, -NH\(_2\)), 7.28-7.36(4H, m, Ar-H), \(^{13}\)C NMR (DMSO-d\(_6\)) : \(\delta\) 48.2, 122.8, 122.3, 125.0, 126.4, 133.2, 151.0, 164.0; FAB Mass : m/z 164.0 (M\(^+\)); CHN analysis : Found: C (58.51%); H (4.91%); N (17.06%); S (19.52%).

**Compound-5b: (5-methoxybenzo[d]thiazol-2-yl)methanamine:**

Yield :49 %, M.P.: 132-133°C; \(^1\)H-NMR(DMSO-d\(_6\)) : \(\delta\) 3.73(3H, s, -CH\(_3\)), 4.33(2H, s, -CH\(_2\)), 5.22(2H, bs, -NH\(_2\)), 7.17-7.20 (1H, dd, Ar-H), 7.34-7.38(1H, dd, Ar-H), 7.39-7.42(1H, dd, Ar-H); \(^{13}\)C NMR (DMSO-d\(_6\)) : \(\delta\) 49.0, 55.2, 102.0, 114.0, 122.6, 134.0, 148.6, 153.8, 163.9; IR(KBr): 3436 cm\(^{-1}\), 1588 cm\(^{-1}\), 1120cm\(^{-1}\), FAB Mass : m/z 194.0 (M\(^+\)); CHN analysis : Found: C (55.58%); H (5.11%); N (14.48%); S (16.56%).

**Compound-5c: (5-butoxybenzo[d]thiazol-2-yl)methanamine:**

Yield :47 %, M.P.: 162-165°C; \(^1\)H-NMR(DMSO-d\(_6\)) : \(\delta\) 0.86-0.88(3H, t, -CH\(_3\)), 1.46-1.52(2H, m, -CH\(_2\)), 1.76-1.80(2H, p, -CH\(_2\)), 4.06-410 (2H, t, -CH\(_2\)), 4.30(2H, s, -CH\(_2\)), 5.10(2H, bs, -NH\(_2\)), 7.21-7.25(1H, dd, Ar-
Synthesis of new derivatives of N-(1H-indol-5-yl)-2-((5-substituted benzo[d]thiazol-2-yl)methanamine:

Yield : 46 %, M.P. : 130-132°C; ^1H-NMR(DMSO-d6) : δ 1.33-1.35(6H, d, 2 x -CH3), 4.35(1H, s, -CH2), 4.74(2H, s, -CH), 5.27(2H, s, -NH2), 7.22-7.24(1H, dd, Ar-H), 7.38-7.41(1H, dd, Ar-H), 7.42-7.45(1H, dd, Ar-H); ^13C NMR (DMSO-d6): δ 22.0, 49.2, 69.5, 102.1, 115.4, 122.7, 133.8, 148.9, 158.6, 163.9; IR (KBr) : 3446 cm⁻¹, 1142 cm⁻¹; FAB Mass : m/z 288.0 (M⁺); CHN analysis : Found:  C (62.53%); H (4.48%); F (6.57%); N (9.74%); S (11.09%). Calc : C (62.48%); H (4.54%); F (6.59%); N (9.72%); S (11.12%).

Compound-5e: (5-((4-fluorobenzyl)oxy)benzo[d]thiazol-2-yl)methanamine:

Yield : 48 %; M.P. : 190-192°C; ^1H-NMR(DMSO-d6) : δ 4.28(2H, s, -CH2-N), 4.88(2H, s, -CH2-O), 5.30(2H, s, -NH2), 6.95-7.46(7H, m, Ar-H); ^13C NMR (DMSO-d6): δ 49.0, 70.0, 102.0,115.3, 122.9,130.1, 133.8, 136.2, 149.9, 156.9, 163.4, 164.0; IR (KBr) : 3455 cm⁻¹, 1466 cm⁻¹, 1142cm⁻¹; FAB Mass : m/z 338.0 (M⁺); CHN analysis : Found:  C (53.06%); H (3.53%); N (8.29%); S (9.45%). Calc : C (53.11%); H (3.57%); N (8.26%); S (9.45%).

Compound-5f: (5-((3,4-dichlorobenzyl)oxy)benzo[d]thiazol-2-yl)methanamine:

Yield : 47 %; M.P. : 206-209°C; ^1H-NMR(DMSO-d6) : δ 4.32(2H, s, -CH2), 4.98(2H, s, -CH2), 5.22(2H,bn, -NH2), 7.24-7.27(1H, dd, Ar-H), 7.30-7.33(1H, dd, Ar-H),7.38-7.41(1H, dd, Ar-H), 7.42-7.45(1H, dd, Ar-H), 7.53-7.56(2H, dd, Ar-H); ^13C NMR (DMSO-d6): δ 49.2,71.3, 102.0, 115.3, 123.0, 128.6,128.9, 133.2, 134.0, 134.1, 137.0, 149.6, 157.1; IR(KBr) : 3450 cm⁻¹, 1572 cm⁻¹, 1106cm⁻¹; FAB Mass : m/z 338.0 (M⁺), 339.0(M+1), 340.0(M+2); CHN analysis : Found:  C (53.06%); H (3.53%); N (8.29%); S (9.45%). Calc : C (53.11%); H (3.57%); N (8.26%); S (9.45%).

Compound-5g: (5-(difluoromethoxy)benzo[d]thiazol-2-yl)methanamine:

Yield : 36 %; M.P. : 138-142°C; ^1H-NMR(DMSO-d6) : δ 4.27(2H, s, -CH2), 5.28(2H, bs, -NH2), 6.56 (1H, s, -CH), 7.17-7.20 (1H, dd, Ar-H), 7.43-7.46 (1H, dd, Ar-H), 7.52-7.55(1H, dd, Ar-H); ^13C NMR (DMSO-d6): δ 48.9, 102.0, 115.2, 115.4, 123.0, 133.9, 158.2, 164.4; IR(KBr) : 3446 cm⁻¹, 1540 cm⁻¹, 1156cm⁻¹; FAB Mass : m/z 230.0 (M⁺); CHN analysis : Found:  C (46.83%); H (3.47%); N (12.23%); S (13.98%).Calc : C (46.95%); H (3.50%); F (16.50%); N (12.17%); O (6.95%); S (13.93%).
Compound-5h: (5-(2,2-difluoroethoxy)benzo[d]thiazol-2-yl)methanamine:

Yield : 49%; M.P. : 148-153°C; 1H-NMR(DMSO-d6) : δ 4.02 (2H, s, -CH2), 4.33(2H, d, -CH2), 5.29 (2H, bs, -NH2), 6.32 (1H, s, -CH), 7.23-7.26 (1H, dd, Ar-H), 7.40-7.43(1H, dd, Ar-H), 7.45-7.48(1H, dd, Ar-H); 13C NMR (DMSO-d6): δ 49.6, 66.0, 102.0, 113.0, 115.3, 122.7, 133.7, 134.1, 152.3, 164.4; IR (KBr) : 3438 cm⁻¹, 1552 cm⁻¹, 1140cm⁻¹; FAB Mass : m/z 244.0 (M'); CHN analysis : Found:  C (52.75%); H (3.89%); O (6.55%); S (17.99%)

Compound-5i: 2-(aminomethyl)benzo[d]thiazole-5-carbonitrile:

Yield : 50%; M.P. : 126-132°C; 1H-NMR(DMSO-d6) : δ 4.49 (2H, s, -CH2), 5.45 (2Hs, -NH2), 7.45-7.48 (1H, dd, Ar-H), 7.70-7.73 (1H, dd, Ar-H), 8.16-8.19(1H, dd, Ar-H); 13C NMR (DMSO-d6): δ 48.6, 108.4, 118.4, 121.0, 126.0, 126.8, 134.0, 152.4, 164.0; IR(KBr) : 3438 cm⁻¹, 2220 cm⁻¹, 1572, 1144cm⁻¹; FAB Mass : m/z 189.0 (M'); CHN analysis : Found:  C (57.06%); H (3.70%); N (22.26%); S (17.01%). Calc :C (57.12%); H (3.73%); N (22.21%); S (16.94%).

Compound-5j: (5-methylbenzo[d]thiazol-2-yl)methanamine:

Yield : 46%; M.P. : 118-121°C; 1H-NMR(DMSO-d6) : δ 2.35 (3H, s, -CH3), 4.48 (2H, s, -CH2), 5.15 (2H, bs, -NH2), 7.27-7.30(1H, dd, Ar-H), 7.65-7.68(1H, dd, Ar-H), 7.75-7.78 (1H, dd, Ar-H); 13C NMR (DMSO-d6): δ 21.2, 48.7, 121.2, 122.6, 123.7, 133.6, 134.1, 152.3, 164.4; IR(KBr) : 3442 cm⁻¹, 1558 cm⁻¹; FAB Mass : m/z 178.0 (M'); CHN analysis : Found:  C (60.66%); H (5.63%); N (15.74%); S (17.97%). Calc :C (60.64%); H (5.65%); N (15.72%); S (17.99%).

Compound-5k: (5-ethylbenzo[d]thiazol-2-yl)methanamine:

Yield : 48%; M.P. : 132-135°C; 1H-NMR(DMSO-d6) : δ 1.12-1.14 (3H, t, -CH3), 2.62-2.65 (2H, s, -CH2), 4.40 (2H, s, -CH2), 5.27(2H, s, -NH2), 7.27-7.30 (1H, dd, Ar-H), 7.64-7.67(1H, dd, Ar-H), 7.72-7.75 (1H, dd, Ar-H); 13C NMR (DMSO-d6): δ 29.0, 40.1, 49.2, 116.4, 121.2, 129.9, 134.0, 156.5, 152.3, 163.8; IR (KBr) : 3465 cm⁻¹, 1582 cm⁻¹; FAB Mass : m/z 192.0 (M'); CHN analysis : Found:  C (62.48%); H (6.31%); N (14.55%); S (16.66%). Calc :C (62.46%); H (6.29%); N (14.57%); S (16.68%).

Compound-5l: (5-fluorobenzo[d]thiazol-2-yl)methanamine:

Yield : 50%; M.P. : 98-100°C; 1H-NMR(DMSO-d6) : δ 4.44 (2H, s, -CH2), 5.13(2Hs, -NH2), 7.20-7.23(1H, dd, Ar-H), 7.48-7.51(1H, dd, Ar-H), 7.85-7.88(1H, dd, Ar-H); 13C NMR (DMSO-d6): δ 49.3, 108.6, 113.2, 121.9, 134.0, 151.1, 163.9; IR (KBr) : 3420 cm₁, 1565 cm⁻¹, 990cm⁻¹; FAB Mass : m/z 182.0 (M'); CHN analysis : Found:  C(52.75%); H (3.89%); N (15.35%); S (17.64%). Calc :C(52.73%); H (3.87%); N (15.37%); S (17.60%).
5m: (5-chlorobenzo[d]thiazol-2-yl)methanamine:

Yield: 46%; M.P.: 88-90°C; $^1$H-NMR (DMSO-d$_6$): $\delta$ 4.47 (2H, s, -CH$_2$), 5.10 (2H, bs, -NH$_2$), 7.48-7.51 (1H, dd, Ar-H), 7.76-7.81 (1H, dd, Ar-H), 7.84-7.87 (1H, dd, Ar-H); $^{13}$C NMR (DMSO-d$_6$): $\delta$ 49.0, 121.2, 122.9, 124.5, 130.5, 133.9, 151.1; IR (KBr): 3328 cm$^{-1}$, 1555 cm$^{-1}$; FAB Mass: m/z 201.0 (M$^+$) 203.0 (M$^+$ + 2); CHN analysis: Found: C (64.26%); H (4.79%); N (16.65%).

Compound-5n: (5-bromobenzo[d]thiazol-2-yl)methanamine:

Yield: 32%; M.P.: 106-108°C; $^1$H-NMR (DMSO-d$_6$): $\delta$ 4.45 (2H, s, -CH$_2$), 5.16 (2H, bs, -NH$_2$), 7.50-7.53 (1H, dd, Ar-H), 7.65-7.68 (1H, dd, Ar-H), 8.06-8.09 (1H, dd, Ar-H); $^{13}$C NMR (DMSO-d$_6$): $\delta$ 48.7, 117.8, 119.4, 127.5, 134.0, 130.2, 131.1, 163.9; IR (KBr): 3428 cm$^{-1}$, 1522 cm$^{-1}$, 640 cm$^{-1}$; FAB Mass: m/z 242.0 (M$^+$), 244.0 (M$^+$ + 2); CHN analysis: Found: C (39.42%); H (2.84%); N (11.61%); S (13.17%).

General procedure for the preparation of N-(1H-indol-5-yl)-2-(((5-substituted benzo[d]thiazol-2-yl)methyl)amino)acetamides (6a-n):

To a solution of 2-chloro-N-(1H-indol-5-yl)acetamide (1.0 m eq) in DMF (3 Vol) was added (5-substituted benzo[d]thiazol-2-yl)methanamine (1.0 m eq), sodium methoxide (1.0 m eq) and stirred at room temperature for 24-35 hrs. The mixture was diluted with water and dichlormethane, then the solid was collected by suction filtration. The filter cake was washed with water. Drying in high vacuum at 50-60°C gave the title compound in 60-70% yield.

Compound-6a: 2-(((benz[d]thiazol-2-ylmethyl)amino)-N-(1H-indol-5-yl)acetamide:

Yield: 63%; M.P.: 168-170°C; IR (KBr): 3400 cm$^{-1}$, 3050 cm$^{-1}$, 1650 cm$^{-1}$; $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.85 (2H, s, -CH$_2$), 4.35 (2H, s, -CH$_2$), 4.86 (1H, bs, -NH), 6.40-6.46 (1H, m, Ar-H), 6.99-7.02 (1H, dd, Ar-H), 7.29-7.43 (3H, m, Ar-H), 7.50-7.56 (1H, m, Ar-H), 7.66-7.70 (1H, m, Ar-H), 7.72-7.75 (1H, m, Ar-H), 7.82-7.85 (1H, m, Ar-H), 7.95 (1H, bs, amide-NH), 10.5 (1H, bs, indole-NH); $^{13}$C NMR (DMSO-d$_6$): $\delta$ 41.0, 57.0, 101.9, 116.2, 117.3, 118.8, 123.0, 125.0, 125.5, 127.0, 127.5, 134.0, 135.0, 139.5, 151.0, 163.9, 169.3; FAB Mass: m/z 336.0 (M$^+$) CHN analysis: Found: C (64.19%); H (4.69%); N (16.72%); S (9.60%).

Compound-6b: N-(1H-indol-5-yl)-2-(((5-methoxybenzo[d]thiazol-2-yl)methyl)amino)acetamide:

Yield: 62%; M.P.: 194-196°C; IR (KBr): 3420 cm$^{-1}$, 3080 cm$^{-1}$, 1640 cm$^{-1}$; $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.74 (3H, s, -OCH$_3$), 3.82 (2H, s, -CH$_2$), 4.20 (2H, s, -CH$_2$), 4.92 (1H, bs, -NH), 6.38-6.43 (1H, m, Ar-H), 7.01-7.03 (1H, dd, Ar-H), 7.19-7.22 (1H, dd, Ar-H), 7.30-7.36 (1H, m, Ar-H), 7.38-7.41 (1H, dd, Ar-H), 7.40-7.43 (1H, dd, Ar-H), 7.49-7.54 (1H, m, Ar-H), 7.65-7.70 (1H, m, Ar-H), 7.83 (1H, bs, amide-NH), 11.02 (1H, bs, indole-NH); $^{13}$C NMR (DMSO-d$_6$): $\delta$ 40.8, 56.0, 57.3, 102.0, 114.0, 115.9, 117.2, 119.0, 123.0, 126.0, 127.4, 133.6, 134.8, 138.9, 150.0, 153.8, 163.6, 168.7; FAB Mass: m/z 366.0 (M$^+$) CHN analysis: Found: C (62.20%); H (4.89%); N (15.35%); S (8.77%).

Calc: C (62.28%); H (4.95%); N (15.29%); O (8.73%); S (8.75%).

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Synthesis of new derivatives of N-(1H-indol-5-yl)-2-((5-substituted benzo[d]thiazol-2-yl)amino)-N-(1H-indol-5-yl)acetamide:

**Compound-6c: 2-(((5-butoxybenz[d]thiazol-2-yl)methyl)amino)-N-(1H-indol-5-yl)acetamide:**

Yield : 65 %, M.P. : 156-157 °C; IR (KBr) : 3440 cm⁻¹, 3070 cm⁻¹, 1646 cm⁻¹; ¹H-NMR(DMSO-d6) : δ 0.89(3H, t, -CH₃), 1.39(2H, m -CH₂), 1.75(2H, m, -CH₂), 3.81(2H, s, -CH₂) 4.06(2H, t, -CH₂), 4.84(1H, bs, -NH), 6.35-6.41(1H, m, Ar-H), 7.06-7.09(1H, dd, Ar-H), 7.23-7.26(1H, dd, Ar-H), 7.31-7.36(1H, m, Ar-H), 7.37-7.45(2H, m, Ar-H), 7.48-7.53(1H, m, Ar-H), 7.69-7.75(1H, m, Ar-H), 7.91(1H, bs, amide-NH), 11.13 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 14.0, 19.3, 31.0, 41.3, 57.0, 69.0, 102.0, 115.4, 115.8, 116.8, 118.6, 122.6, 124.7, 126.8, 133.7, 134.7, 140.2, 150.0, 163.5, 168.9; FAB Mass : m/z 408.0 (M⁺); CHN analysis : Found: C (64.63%); H (5.87%); N (13.75%); S (7.87%). Calc : C (64.68%); H (5.92%); N (13.71%); O (7.83%); S (7.85%).

**Compound-6d: N-(1H-indol-5-yl)-2-(((5-isopropoxybenz[d]thiazol-2-yl)methyl)amino)acetamide:**

Yield : 62 %, M.P. : 212-214 °C; IR(KBr) : 3388 cm⁻¹, 1652 cm⁻¹, 3068 cm⁻¹; ¹H-NMR(DMSO-d6) : 1.20 (6H, t, 2 x CH₃), 3.92(2H, s, -CH₂), 4.19(2H, s, -CH₂), 4.75(1H, m, CH), 4.93(1H, bs, -NH), 6.42-6.47(1H, m, Ar-H), 6.86-6.89 (1H, dd, Ar-H), 7.22-7.25(1H, dd, Ar-H),7.27-7.32 (1H, m, Ar-H), 7.36-7.43(2H, m, Ar-H), 7.46-7.51(1H, m, Ar-H), 7.62-7.67(1H, m, Ar-H), 7.93(1H, bs, amide-NH), 10.88 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 22.0, 39.7, 58.0, 70.0, 102.0, 114.7, 115.5, 116.5, 118.3, 123.0, 125.4, 127.3, 133.6, 135.0, 138.7, 149.3, 158.5, 164.5, 168.9; FAB Mass : m/z 394.0 (M⁺); CHN analysis : Found: C (63.86%); H (5.54%); N (14.21%); S (8.09%). Calc : C (63.94%); H (5.62%); N (14.25%); S (8.18%).

**Compound-6e:**

2-(((5-(4-fluorobenzyl)oxy)benz[d]thiazol-2-yl)methyl)amino)-N-(1H-indol-5-yl)acetamide:

Yield : 60 %, M.P. : 242-243 °C; IR(KBr) : 3498 cm⁻¹, 3058 cm⁻¹, 1660 cm⁻¹; ¹H-NMR(DMSO-d6) : 3.85(2H, s, -CH₂), 4.17(2H, s, -CH₂), 4.83(2H, s, -CH₂-O), 4.81(1H, bs, -NH), 6.44-6.50(1H, m, Ar-H), 6.92-7.03 (3H, m, Ar-H), 7.24-7.27(1H, dd, Ar-H),7.32-7.38 (1H, m, Ar-H), 7.38-7.45(3H, m, Ar-H), 7.48-7.54(2H, m, Ar-H), 7.69-7.74(1H, m, Ar-H), 8.01(1H, bs, amide-NH), 11.30 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 39.8, 56.9, 70.0, 101.7, 115.0, 115.3, 116.3, 117.0, 119.4, 122.7, 125.0, 126.7, 129.8, 134.0, 135.0, 136.3, 139.5, 149.9, 163.0, 163.8, 169.0; FAB Mass : m/z 460.0 (M⁺); CHN analysis : Found: C (65.16%); H (4.57%); N (12.20%); S (6.98%). Calc : C (65.20%); H (4.60%); N (12.17%); S (6.96%).

**Compound-6f:**

2-(((5-(3,4-dichlorobenzyl)oxy)benz[d]thiazol-2-yl)methyl)amino)-N-(1H-indol-5-yl)acetamide:

Yield : 63 %, M.P. : 198-199°C; IR(KBr) : 3410 cm⁻¹, 3035 cm⁻¹, 1620 cm⁻¹; ¹H-NMR(DMSO-d6) : 3.88(2H, s, -CH₂), 4.20 (2H, s, -CH₂), 4.97(1H, bs, -NH), 6.42-6.47(1H, m, Ar-H), 6.89-6.93 (1H, dd, Ar-H), 7.18-7.21(1H, dd, Ar-H),7.27-7.35 (2H, m, Ar-H), 7.40-7.44(1H, dd, Ar-H), 7.48-7.57(4H, m, Ar-H), 7.62-7.68(1H, m, Ar-H), 7.96 (1H, bs, amide-NH), 11.05 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 40.0, 57.0, 70.8, 102.0, 102.2, 115.4, 116.4, 117.3, 118.6, 122.0, 124.9, 127.4, 128.7, 128.9, 129.9, 133.2, 133.6, 135.0, 137.0, 139.5, 150.2, 157.0, 163.6, 168.4; FAB Mass : m/z 510.0 (M⁺), 511.0(M+1), 512.0(M+2); CHN analysis : Found: C (58.63%); H (3.86%); N (11.04%); S (6.35%). Calc :C (58.71%); H (3.94%); N (10.96%); S (6.27%).

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Synthesis of new derivatives of N-(1H-indol-5-yl)-2-(((5-substituted benzo[d]thiazol-2-yl)methyl)(amino)N-(1H-indol-5-yl)acetamide:

Compound-6g: 2-(((5-(difluoromethoxy)benzo[d]thiazol-2-yl)methyl)(amino)N-(1H-indol-5-yl)acetamide:

Yield: 62 %; M.P.: 150-152°C; IR (KBr): 3420 cm⁻¹, 3080 cm⁻¹, 1688 cm⁻¹, 930 cm⁻¹;
¹H-NMR(DMSO-d₆): δ 3.97(2H, s, -CH₂), 4.17 (2H, s, -CH₂), 4.96(1H, bs, -NH), 6.37-6.42(1H, m, Ar-H), 6.56(1H, s, Ar-H), 6.99-7.02(1H, dd, Ar-H), 7.17-7.20(1H, dd, Ar-H), 7.28-7.34(1H, m, Ar-H), 7.43-7.47(1H, dd, Ar-H), 7.50-7.57(4H, m, Ar-H), 7.65-7.71(1H, m, Ar-H), 7.97 (1H, bs, amide-NH), 10.98 (1H, bs, indole-NH); ¹³C NMR (DMSO-d₆): δ 41.2, 56.9, 102.0, 102.2, 114.4, 115.0, 116.1, 117.0, 118.9, 123.0, 125.7, 127.2, 134.0, 135.0, 140.0, 149.8, 158.2, 163.5, 169.1; FAB Mass: m/z 402.0 (M⁺); CHN analysis: Found: C 56.67%; H 3.96%; N 13.98%; S (8.13%). Calc :C 56.71%; H (4.01%); F (9.44%); N (13.92%); O (7.95%); S (7.97%).

Compound-6h: 2-(((5-(2,2-difluoromethoxy)benzo[d]thiazol-2-yl)(methyl)(amino)N-(1H-indol-5-yl)acetamide:

Yield: 65 %; M.P.: 222-224°C; IR(KBr): 3465 cm⁻¹, 3070 cm⁻¹, 1638 cm⁻¹, 950 cm⁻¹;
¹H-NMR(DMSO-d₆): 3.90(2H, s, -CH₂), 4.00 (2H, d, -CH₂), 4.22 (2H, s, -CH₂), 4.82(1H, bs, -NH), 6.32(1H, t, -CH), 6.40-6.45(1H, m, Ar-H), 6.97-7.00 (1H, dd, Ar-H), 7.25-7.28 (1H, dd, Ar-H), 7.33-7.38 (1H, m, Ar-H), 7.39-7.45 (2H, m, Ar-H), 7.50-7.56 (1H, m, Ar-H), 7.70-7.75(1H, m, Ar-H), 8.07 (1H, bs, amide-NH), 11.23 (1H, bs, indole-NH); ¹³C NMR (DMSO-d₆): δ 40.9, 56.5, 65.7, 102.0, 102.2, 112.8, 115.0, 116.4, 116.9, 119.0, 123.0, 126.0, 127.1, 133.7, 135.0, 139.4, 150.0, 157.1, 164.0, 169.3; FAB Mass: m/z 416.0 (M⁺); CHN analysis: Found: C 57.70%; H (4.38%); F (9.10%); N (13.43%); O (7.70%); S (7.68%). Calc :C 57.68%; H (4.36%); F (9.12%); N (13.45%); O (7.68%); S (7.70%).

Compound-6i: 2-(((5-(cyanobenzo[d]thiazol-2-yl)(methyl)(amino)N-(1H-indol-5-yl)acetamide:

Yield: 60 %; M.P.: 196-197°C; IR(KBr): 3354 cm⁻¹, 3042 cm⁻¹, 1658 cm⁻¹, 2220 cm⁻¹;
¹H-NMR(DMSO-d₆): 3.96(2H, s, -CH₂), 4.39 (2H, s, -CH₂), 5.01 (1H, bs, -NH), 6.45-6.50 (1H, m, Ar-H), 6.95-6.99 (1H, dd, Ar-H), 7.30-7.36 (1H, m, Ar-H), 7.45-7.48 (1H, dd, Ar-H), 7.52-7.58 (1H, m, Ar-H), 7.72-7.77(1H, m, Ar-H), 7.91-7.96 (1H, m, Ar-H), 8.12 (1H, bs, amide-NH), 11.50 (1H, bs, indole-NH); ¹³C NMR (DMSO-d₆): δ 38.7, 56.7, 102.0, 108.3, 116.0, 117.4, 118.3, 121.0, 125.3, 126.0, 126.9, 127.4, 134.0, 135.0, 139.6, 152.3, 163.7, 169.0; FAB Mass: m/z 361.0 (M⁺); CHN analysis: Found: C (63.09%); H (4.08%); N (19.42%); S (8.95%). Calc :C (63.14%); H (4.18%); N (19.38%); O (4.43%); S (8.87%).

Compound-6j: N-(1H-indol-5-yl)-2-(((5-(methylbenzo[d]thiazol-2-yl)(methyl)(amino)acetamide:

Yield: 65%; M.P.: 178-180°C; IR (KBr): 3430 cm⁻¹, 3065 cm⁻¹, 1670 cm⁻¹;
¹H-NMR(DMSO-d₆): 2.34 (3H, s, -CH₃), 3.87(2H, s, -CH₂), 4.28 (2H, s, -CH₂), 4.75 (1H, bs, -NH), 6.43-6.45 (1H,dd, Ar-H), 7.24-7.27 (1H, dd, Ar-H), 7.33-7.39 (2H, m, Ar-H), 7.43-7.46 (1H, dd, Ar-H), 7.90-7.93 (1H, dd, Ar-H), 7.99-8.05(2H, m, Ar-H), 8.86 (1H, bs, amide-NH), 11.45 (1H, bs, indole-NH); ¹³C NMR (DMSO-d₆): δ 21.0, 40.9, 57.3, 102.0, 115.9, 116.6, 121.0, 123.0, 123.7, 126.0, 127.0, 134.0, 134.1, 135.0, 139.5, 152.0, 163.5, 168.5; FAB Mass: m/z 350.0 (M⁺); CHN analysis: Found: C (65.08%); H (5.13%); N (16.03%); S (9.21%). Calc :C (65.12%); H (5.18%); N (15.99%); O (4.57%); S (9.15%).

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Synthesis of new derivatives of N-(1H-indol-5-yl)-2-(((5-substituted benzo[d]thiazol-2-yl)amino)-N-(1H-indol-5-yl)acetic acid:

Yield : 62%; M.P. : 180-181°C; IR(KBr) : 3360 cm⁻¹, 3075 cm⁻¹, 1657 cm⁻¹; Yield : 65%; M.P. : 178-180°C; IR (KBr) : 3430 cm⁻¹, 3065 cm⁻¹, 1670 cm⁻¹; ¹H-NMR(DMSO-d6) : 1.20(3H, t, -CH₃), 2.60 (2H, q, -CH₂), 3.78(2H, s, -CH₂), 3.95 (2H, s, -CH₂), 4.77 (1H, bs, -NH), 6.44-6.47 (1H,dd, Ar-H), 7.25-7.28 (1H, dd, Ar-H), 7.38-7.46 (3H, m, Ar-H), 7.67-7.90 (3H, m, Ar-H). 8.35 (1H, bs, amide-NH), 11.22 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 14.8, 32.0, 51.0, 53.0, 102.4,110.0, 111.2, 112.6, 119.0, 122.0, 124.0 126.0, 128.3,130.0 131.0, 134.0, 154.2, 158.0.

Compound-6b: 2-(((5-fluorobenzo[d]thiazol-2-yl)methylamino)-N-(1H-indol-5-yl)acetamide:

Yield : 61%; M.P. : 182-184°C; IR (KBr) : 3426 cm⁻¹, 3066 cm⁻¹, 1650 cm⁻¹; ¹H-NMR(DMSO-d6) : 3.89 (2H, s, -CH₂), 4.30 (2H, s, -CH₂), 4.99 (1H, bs, -NH), 6.48-6.53 (1H,dd, Ar-H), 7.24-7.29 (2H, m, Ar-H), 7.39-7.45 (2H, m, Ar-H), 7.73-7.95 (2H, m, Ar-H), 8.05-8.08( 1H, dd, Ar-H), 8.63 (1H, bs, amide-NH), 11.60 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 48.1, 56.8, 102.4,108.3, 110.0, 111.3, 112.6, 114.6, 123.5, 124.0 128.3,130.0 131.0, 134.0, 154.2, 158.0, 168.3, 169.5; FAB Mass : m/z 354.0 (M⁺); CHN analysis : Found: C(61.02%); H (4.29%); F (5.38%); N (15.78%); O (4.51%); S (9.05%); Calc :C (61.00%); H (4.27%); F (5.36%); N (15.81%); O (4.51%); S (9.05%).

Compound-6d: 2-(((5-chlorobenzo[d]thiazol-2-yl)methylamino)-N-(1H-indol-5-yl)acetamide:

Yield : 62%; M.P. : 188-190°C; IR (KBr) : 3432 cm⁻¹, 3058 cm⁻¹, 1642 cm⁻¹; ¹H-NMR(DMSO-d6) : 3.75 (2H, s, -CH₂), 4.09 (2H, s, -CH₂), 4.90(1H, bs, -NH), 6.41-6.45 (1H,dd, Ar-H), 7.23-7.27 (1H, dd, Ar-H), 7.33-7.37 (1H, dd, Ar-H), 7.46-7.54 (2H, m, Ar-H), 7.96-8.16 (3H, m, Ar-H), 8.40 (1H, bs, amide-NH), 11.55 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 44.0, 55.8, 102.4, 115.9, 117.0, 118.8,120.6, 126.0, 127.0, 134.0,135.0, 139.3 , 151.1, 164.8, 169.5; FAB Mass : m/z 370.05 (M⁺), 372.05(M+2); CHN analysis : Found: C (58.24%); H (4.03%); N (15.17%); S (8.76%). Calc :C (58.30%); H(4.08%); N (15.11%); S (8.65%).

Compound-6n: 2-(((5-bromobenzo[d]thiazol-2-yl)methylamino)-N-(1H-indol-5-yl)acetamide:

Yield : 63%; M.P. : 230-233°C; IR : 3475 cm⁻¹, 3048 cm⁻¹, 1668 cm⁻¹; ¹H-NMR(DMSO-d6) : 3.86 (2H, s, -CH₂), 4.17 (2H, s, -CH₂), 4.86(1H, bs, -NH), 6.46-6.49 (1H,dd, Ar-H), 7.27-7.31 (1H, dd, Ar-H), 7.34-7.46 (2H, dd, Ar-H), 7.70-7.93 (2H, m, Ar-H), 8.00-8.40( 2H, m, Ar-H), 8.56 (1H, bs, amide-NH), 11.92 (1H, bs, indole-NH); ¹³C NMR (DMSO-d6): δ 45.8, 54.9, 102.2,116.4, 117.3, 118.0, 119.0, 126.0, 127.0,128.0, 133.0,134.0, 135.0,140.0 , 150.9, 164.0, 168.7; FAB Mass : m/z 412.4 (M⁺), 416.2(M+2); CHN analysis :Found: C (52.04%); H (3.62%); N (13.51%); S (7.74%); Calc :C (52.06%); H (3.64%); N (13.49%); S (7.72%).

Antibacterial Activity: The antibacterial activity was assayed by agar plate disc diffusion method at the concentration of 50 µg per disk. All the synthesized compounds were tested in vitro for their antibacterial activity against microorganisms such as Staphylococcus aureus, Bacillus subtilis (gram positive), Escherichia coli, and Pseudomonas aeruginosa (gram negative) strains. Each test compounds were dissolved in

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dimethylsulfoxide (DMSO) to get a concentration of 100 µg/ml. The disc (6 mm in diameter) was impregnated with 5 µL of each test solution to get 50 µg/disc, air dried and placed on the agar medium, previously seeded with 0.2 ml of broth culture of each organism for 18 hours. The plates were incubated at 37 °C for 24 hours and the inhibition zones measured in mm. Discs impregnated with DMSO were used as a control and ampicillin discs as antibacterial reference standard.

**Antifungal activity:** The antifungal activity was assayed by the Sabouraud dextrose agar media plate disc diffusion method at a concentration of 50 µg per disk. All the synthesized compounds were tested in vitro for their antifungal activity against microorganisms such as Aspergillus niger and Candida albicans. Each test compound was dissolved in dimethylsulfoxide (DMSO) to get a concentration of 10 mg/ml. The Pharmaceuticals 2010, 3 2424 disc (6 mm in diameter) was impregnated with 5 µL of each test solution to get 50 µg/disc; air dried and placed on the Sabouraud dextrose agar media, previously seeded with 0.2 ml of broth culture of each organism for 18 hours. The plates were incubated at 22 °C for 48 hours and the inhibition zones measured in mm. Discs impregnated with DMSO were used as a negative control and fluconazole discs as antifungal reference standard.

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**References**

Synthesis of new derivatives of N-(1H-indol-5-yl)-2-(((5-substituted benzol[d]hiazol-2-yl)methyl)amino)acetamides and their antimicrobial activity.