Design and Synthesis of Benzodiazepines Bearing Benzimidazole / Benzothiazole and Indole Moieties as A Potent Antimicrobial and Antioxidant Agents

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ABSTRACT

In the present work 2-((1H-benzo[d]imidazol-2-yl)thio)-N-4-(4-(1H-indol-3-yl)-8-methyl-1H-benzo[b][1,4]diazepin-2-yl)phenyl)acetamide 3a-d, N-44-(1H-indol-3-yl)-8-methyl-1H-benzo[b][1,4]diazepin-2-yl)phenyl)-2-(5-methoxy-1H-benzo[d]imidazol-2-yl)thio)acetamide 4a-d and N-(4-(1H-indol-3-yl)-8-methyl-1H-benzo[b][1,4]diazepin-2-yl)phenyl)-2-(benzo[d]thiazol-2-ylthio) acetamide 5a-d were synthesized in good yield in in-situ by cyclization of chalcones with substituted ortho-phenylenediamine. The chalcones were in turn prepared by Claisen–Schmidt condensation 2-(1H-benzo[d]imidazol-2-ylthio)-N-(4-acetylphenyl) acetamide and various 2, 5-disubstituted indole-3-carboxaldehydes in the presence of piperidine. The structures of all the newly synthesized compounds were characterized by their IR, ^1H^NMR, mass spectral studies and elemental analysis. All these compounds were screened for their in-vitro antimicrobial activity by agar plate diffusion method, Antioxidant activities: like, 1,1-Diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA), Ferric ions (Fe^{3+}) reducing antioxidant power (FRAP), Ferrous (Fe^{2+}) metal ion chelating activity. Some of the compounds have shown potent anti-microbial activity against all the screened bacteria and fungi and some have exhibited very good antioxidant activity.

Keywords: Benzodiazepine, Indole, Benzimidazole/Benzothiazole, Antimicrobial, Antioxidant

INTRODUCTION

Benzodiazepines and their derivatives are a very important class of bioactive compounds because of their diverse pharmacological properties. They are widely used as antidepressants, anti-convulsant, analgesic, hypnotic and sedative [1]. This compound possesses anti-inflammatory [2], antimicrobial, antioxidant [3] and anticancer activity [4]. It acts as an inhibitor of respiratory syncytial virus [5]. 1, 4-benzodiazepine analogues have been demonstrated as anticonvulsants, muscle relaxants, blood pressure lowering and CNS depressant agents [6]. Alongside, indoles and its biheterocycles are featured widely in a wide variety of biological and pharmacologically active compounds [7]. The indole derivatives are known to possess anticancer, antioxidant, antitumor and anti-HIV [8-11] activities. Benzimidazole is an essential pharmacophore and a privileged structure in medicinal chemistry. It has been found to possess antioxidant, anti-inflammatory, Diuretic, antiviral, anticonvulsant, anti diabetic [12-17] activities. Benzothiazole is also a heterocyclic compound, with various biological activities. This heterocycle possess diverse biological activities such as antitumor, anticancer, antifungal and antibacterial [18-21] activities. In the view of above mentioned facts we describe herein the design, synthesis and characterization of some benzodiazepines bearing benzimidazole / benzothiazole and indole moieties as a potent antimicrobial and antioxidant agents.

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC using silica gel-G coated aluminum plates (Merck) and spots were visualized by exposing the dry plates to iodine vapors. The IR (KBr) spectra were recorded on a Perkin-Elmer spectrum one FTIR spectrometer. The ^1H-NMR (DMSO-d_6) spectra recorded on a Bruker NMR (400 MHz) and the chemical shifts were expressed in ppm (δ scale) downfield from TMS. Mass spectral data were recorded by electron impact method on JEOL GCMATE II GC-MS mass spectrometer. Elemental analysis was carried out using Flash EA 1112 series elemental analyzer. All the compounds gave C, H and N analysis within ±0.5% of the theoretical values.

Procedure

General procedure for the synthesis of N-(4-acetylphenyl)-2-chloroacetamide (2) was prepared by following the literature method [22]
N-(4-acetylphenyl)-2-chloroaacetamide (2): (0.01 mol) obtained was further reacted with 2-mercaptobenzimidazole, 2-mercapto-5-methoxy benzimidazole and 2-mercapto benzothiazole (0.01 mol). The reaction was stirred for 4 h at room temperature in the presence of K₂CO₃ (0.02 mol) and acetone (20 ml) was used as the reaction medium. After the completion of reaction monitored on TLC using Toluene: Acetone (8:2) as mobile phase, product was poured into water and stirred vigorously for 1 h. The separated precipitates were collected and dried. The product was recrystallized from ethanol.

2-(1H-benzo[d]imidazole-2-ylthio)-N-(4-acetylphenyl)acetamide (3): Yield 86% (Ethanol); M.P 210°C; IR (KBr) (νmax in cm⁻¹): 1409, 1650, 2850, 3110, 3285, 3400; ¹H-NMR (DMSO-d₆ + CDCl₃) (ppm): 2.50 (S, 3H, -CH₃), 4.32 (S, 2H, -CH₂), 7.10-7.96 (m, 8H, Ar-H), 10.85 (S, 1H, -NH), 12.86 (S, 1H, benzimidazole -NH); Anal. Calcd for C₁₅H₁₂N₂O₂S (325): C, 62.75; H, 4.65; N, 12.91. Found: C, 62.74; H, 4.67; N, 12.90.

N-(4-acetylphenyl)-2-((5-methoxy-1H-indol-3-yl)-3-methyl-1H-benz[d]imidazo[2,1-b]thiazol-5-yl)acetamide (4): Yield 80% (Ethanol); M.P 152°C; IR (KBr) (νmax in cm⁻¹): 1406, 1625, 2862, 2992, 3285, 3379. ¹H-NMR (DMSO-d₆ + CDCl₃) (ppm): 2.50 (S, 3H, -CH₃), 3.76 (S, 3H, OCH₃), 4.32 (S, 2H, -CH₂), 6.72-8.22 (m, 7H, Ar-H), 10.88 (S, 1H, -NH), 12.48 (S, 1H, benzimidazole -NH); Anal. Calcd for C₁₆H₁₉N₃O₃S (355): C, 60.83; H, 4.82; N, 11.82. Found: C, 60.81; H, 4.85; N, 11.81.

N-(4-acetylphenyl)-2-(benzothiazol-2-ylthio)acetamide (5): Yield 77% (Ethanol); M.P 130°C; IR (KBr) (νmax in cm⁻¹): 1457, 1625, 2850, 2992, 3276, 3380. ¹H-NMR (DMSO-d₆ + CDCl₃) (ppm): 2.50 (S, 3H, -CH₃), 4.40 (S, 2H, -CH₂), 7.29-7.92 (m, 8H, Ar-H), 10.71 (S, 1H, -NH); Anal. Calcd for C₁₅H₁₂N₂O₂S (342): C, 59.63; H, 4.12; N, 8.18. Found: C, 59.61; H, 4.15; N, 8.19.

The Claisen–Schmidt condensation of an equimolar mixture of 2-(1H-benzo[d]imidazole-2-ylthio)-N-(4-acetylphenyl) acetamide (0.01 mol) and various 2,5-disubstituted indole-3-carboxaldehydes (0.01 mol) were refluxed (3-4 h) in ethanol (15-20 ml) in the presence of piperidine. After 4 h substituted ortho-phenylenediamine and a catalytic amount of acetic acid was added to the reaction mixture and was further refluxed (7-8 h). The completion of the reaction was monitored by TLC. The product was poured in ice cold water. The product obtained was filtered and purified by ethanol.

N-(4-acetylphenyl)-2-(4-methyl-1H-indol-3-yl)-3-methyl-1H-benz[d]imidazo[2,1-b]thiazol-5-yl)acetamide (6a-d): The Claisen–Schmidt condensation of an equimolar mixture of 2-(1H-benzo[d]imidazole-2-ylthio)-N-(4-acetylphenyl) acetamide (0.01 mol) and various 2,5-disubstituted indole-3-carboxaldehydes (0.01 mol) were refluxed (3-4 h) in ethanol (15-20 ml) in the presence of piperidine. After 4 h substituted ortho-phenylenediamine and a catalytic amount of acetic acid was added to the reaction mixture and was further refluxed (7-8 h). The completion of the reaction was monitored by TLC. The product was poured in ice cold water. The product obtained was filtered and purified by ethanol.

N-(4-acetylphenyl)-2-(4-methyl-1H-indol-3-yl)-3-methyl-1H-benz[d]imidazo[2,1-b]thiazol-5-yl)acetamide (6a): Yield 70 % (Ethanol); M.P 176-178°C; IR (KBr) (νmax in cm⁻¹): 1673, 2838, 3098, 3110, 3318, 3409; ¹H-NMR (DMSO-d₆ + CDCl₃) (ppm): 2.4 (S, 3H, -CH₃), 4.4 (S, 2H, -CH₂), 7.8-8.2 (m, 18H, 17Ar-H, diazepine -NH), 10.1 (S, 1H, indole -NH), 11.2 (S, 1H, -NH), 12.7 (S, 1H, benzimidazole -NH). MS: m/z = 554 [M]⁺; Anal. Calcd for C₁₅H₁₄N₂O₂S (554): C, 71.46; H, 4.72; N, 15.15. Found: C, 71.43; H, 4.69; N, 15.12.
The Antimicrobial activity

Biological activities

Antimicrobial activity

The in-vitro antimicrobial activity of the synthesized compounds 6a-d, 7a-d, 8a-d was carried out against bacterial strains *Escherichia coli* (MTCC-723), *Staphylococcus aureus* (ATCC-29513), and *Pseudomonas aeruginosa* (MTCC-1688) and fungal species, *Aspergillus niger* (MTCC-281), *Aspergillus flavus* (MTCC-1973), and *Aspergillus oryzae* (MTCC-3567) by cup plate method [23] using nutrient agar and PDA as medium, respectively. The holes of 6 mm diameter were punched carefully using a sterile cork borer and these were filled with test solution (1000 μg/ml in DMF) and DMF used as control. The plates were incubated at 37°C for 24 and 72 h in case antibacterial and antifungal activity,
Antioxidant activity assay

DPPH free radical scavenging activity

The free radical scavenging activity (RSA) of all the compounds at concentrations of 25, 50, 75 and 100 µg/ml was carried out in the presence of freshly prepared solution of stable free radical DPPH (0.04% w/v) following Hatano’s method [24] using 2-tert-butyl-4-methoxyphenol (butylatedhydroxy anisole, BHA), 2-(1,1-dimethylethyl)-1,4-benzenediol (2-tert-butyl hydroquinone, TBHQ) and Ascorbic acid (AA) as standards. All the test analyses were performed on three replicates and the results are averaged. The results in percentage are expressed as the ratio of absorption decrease of DPPH in the presence of test compounds and absorption of DPPH in the absence of test compounds at λ 517 nm on ELICO SL 171 Mini Spec. spectrophotometer. The percentage scavenging activity of the DPPH free radical was measured using the following equation:

\[
\text{% of DPPH RSA} = \frac{\text{Absorbance of Control} - \text{Absorbance of Sample}}{\text{Absorbance of Control}} \times 100
\]

The results are shown in Figure 1.

Ferric ions (Fe\(^{3+}\)) reducing antioxidant power (FRAP)

The Ferric ions (Fe\(^{3+}\)) reducing antioxidant power (FRAP) of the synthesized compounds were determined according to the literature method [25]. Different concentrations of samples (25, 50, 75 and 100 µg/ml) in DMSO (1 ml) were mixed with phosphate buffer (2.5 ml, 0.2 M, pH=6.6) and potassium ferricyanide (2.5 ml, 1%). The mixture was incubated at 50°C for 20 min. After which a portion of trichloroacetic acid (2.5 ml, 10%) was added to the mixture and centrifuged for 10 min, at 1000 Xg. The upper layer of solution (2.5 ml) was mixed with distilled water (2.5 ml) and ferric chloride (0.5 ml, 0.1 %). Then absorbance at λ 700 nm was measured in a spectrophotometer. The higher absorbance of the reaction mixture indicated greater reducing power. The results are shown in Figure 2.

Ferrous (Fe\(^{2+}\)) metal ion chelating activity

The chelating activity of ferrous iron of synthesized compounds was estimated by following reported method [26]. The test samples (25, 50, 75 and 100 µg/ml) in ethanolic solution (0.4 ml) were added to a solution of FeCl\(_2\) (0.05 ml, 2 mmol). The reaction was initiated by the addition of ferrozine (0.2 ml, 5 mmol) and the total volume was adjusted to 4 ml with ethanol. Ferrozine reacted with the divalent iron form stable magenta complex species that were very soluble in water. The mixture was shaken vigorously and kept at room temperature for 10 min. Then the absorbance of the solution was measured spectrophotometrically at λ 562 nm. All test analyses were run in triplicate and averaged. The percentage of inhibition of the ferrozine Fe\(^{2+}\) complex formations was calculated using the following formula:

\[
\text{% of Ferrous ion Chelating} = \frac{\text{Absorbance of Control} - \text{Absorbance of Sample}}{\text{Absorbance of Control}} \times 100
\]

The results are shown in Figure 3.

RESULTS AND DISCUSSION

In the present investigation, 4-aminoacetophenone (1) was reacted with chloroacetylchloride to form an intermediate N-(4-acetylphenyl)-2-chloroacetamide (2), which on reaction with 2-mercaptobenzimidazole, 2-mercaptop-5-methoxy benzimidazole and 2-mercaptop benzothiazole, resulted in the formation of 2-(1H-benzo[d]imidazol-2-ylthio)N-(4-acetylphenyl)acetamide (3), N-(4-acetylphenyl)-2-((5-methoxy-1H-benzol[d]imidazol-2-ylthio)acetamide (4) and N-(4-acetylphenyl)-2-(benzol[d]thiazol-2-ylthio)acetamide (5) respectively by following the literature method [22].

Compound 3, 4 and 5 on Claisen–Schmidt condensation with various 2,5-disubstituted indole-3-carboxaldehydes were refluxed in ethanol in presence of piperidine for 4 h. After 4 h substituted ortho-phenylenediamine and catalytic amount of acetic acid was added to reaction mixture and was further refluxed (7-8 h) to yield the products 2-((1H-benzo[d]imidazol-2-ylthio)-N-(4-(4-(1H-indol-3-yl)-8-methyl-1H-benzol[b][1,4]diazepin-2-yl)phenyl)acetamide 6a-d, N-((4-(1H-indol-3-yl)-8-methyl-1H-benzol[b][1,4]diazepin-2-yl)phenyl)-2-((5-methoxy-1H-benzol[d]imidazol-2-ylthio)acetamide 7a-d and N-((4-(1H-indol-3-yl)-8-methyl-1H-benzol[b][1,4]diazepin-2-yl)phenyl)-2-(benzol[d] thiazol -2-ylthio) acetamide 8a-d respectively. The structures of all the novel compounds were confirmed by IR, \(^{1}\)H NMR, and mass spectral studies and elemental data. The synthetic approach is outlined in Scheme 1.

The physical data of the compounds are presented in Table 1. The structures of the compounds were confirmed by IR, \(^{1}\)H-NMR, mass spectral studies and elemental data. The IR spectrum of 6a exhibited absorption band at 3409 cm\(^{-1}\), 3318 cm\(^{-1}\), 3110 cm\(^{-1}\) and 3098 cm\(^{-1}\) for NH stretching frequency of indole, benzimidazole, amide and diazepine respectively. The absorption band at 1673 cm\(^{-1}\) corresponds to C=O stretching of amide. In the \(^{1}\)H-NMR spectrum, the compound 6a showed a singlet peaks at 12.27, 11.2 and 10.1 ppm ascribed to NH protons of benzimidazole, amide and indole respectively. In addition to this, seventeen aromatic protons and one proton of diazepine NH resonated as a multiplet in the region 7.8-8.2 ppm. The singlet at 4.4 ppm and 2.4 ppm is due to the two protons of methylene group and three protons of methyl group respectively. Further, the mass spectrum of 6a showed a molecular ion peak M\(^+\) at m/z 554, which confirms its molecular weight and is in good agreement with nitrogen rule.
Scheme 1: Synthesis of compounds 3, 4, 5, 6a-d, 7a-d and 8a-d.

Reagents; (a) substituted indole aldehyde; (b) piperidine; (c) acetic acid; (d) 4-methyl-orthophenylenediamine
Antimicrobial activity

Table 2: Antibacterial activity, size of inhibition zone (mm) formed at different concentrations (1000, 500, 250 and 125 µg/ml) of synthesized compounds 6a-d, 7a-d and 8a-d

| Compound | Zone of inhibition in mm |
|----------|-------------------------|
|          | Staphylococcus aureus | Escherichia coli | Pseudomonas aeruginosa |
|          | 1000 | 500 | 250 | 125 | 1000 | 500 | 250 | 125 | 1000 | 500 | 250 | 125 |
| 6a       | 11   | 13  | 13  | 12  | 11   | 12  | 12  | 13  | 11   | 12  | 13  | 12  |
| 6b       | 15   | 15  | 14  | 15  | 16   | 16  | 15  | 16  | 15   | 15  | 15  | 14  |
| 6c       | 13   | 13  | 12  | 11  | 11   | 12  | 13  | 13  | 12   | 13  | 12  | 12  |
| 6d       | 14   | 15  | 16  | 16  | 15   | 15  | 16  | 15  | 15   | 14  | 14  | 15  |
| 7a       | 15   | 13  | 14  | 15  | 15   | 14  | 15  | 15  | 13   | 14  | 15  | 14  |
| 7b       | 17   | 17  | 16  | 16  | 16   | 16  | 17  | 17  | 17   | 16  | 16  | 15  |
| 7c       | 16   | 15  | 15  | 14  | 14   | 15  | 14  | 15  | 15   | 14  | 14  | 14  |
| 7d       | 16   | 15  | 16  | 16  | 16   | 16  | 15  | 15  | 15   | 15  | 15  | 14  |
| 8a       | 14   | 14  | 15  | 15  | 14   | 15  | 15  | 15  | 15   | 14  | 14  | 14  |
| 8b       | 17   | 17  | 17  | 16  | 16   | 16  | 15  | 15  | 16   | 16  | 16  | 16  |
| 8c       | 15   | 15  | 16  | 16  | 15   | 15  | 14  | 14  | 14   | 13  | 14  | 13  |
| 8d       | 16   | 16  | 16  | 16  | 15   | 15  | 16  | 15  | 15   | 14  | 14  | 14  |
| Sterptomycin | 17  | 17  | 17  | 17  | 17   | 16  | 16  | 16  | 15   | 16  | 16  | 15  |

Note: Values are expressed as mean (n=3)

The analysis of antibacterial screening (Table 2) revealed that all compounds tested have moderate to high antibacterial activity as compared to the standard drug streptomycin. Compounds 6d, 7b-d, 8b-d have showed excellent antibacterial activity against the tested microorganism S. aureus (ATCC-29513). Compounds 6b, 6d, 7a-d, and 8a-d have exhibited good activity against E.coli (MTCC-723). Whereas, the compounds 6b, 6d, 7a-d, and 8a-d displayed good activity against P. aeruginosa (MTCC-1688).

Table 3: Antifungal activity, size of inhibition zone (mm) formed at different concentrations (1000, 500, 250 and 125 µg/ml) of synthesized compounds 6a-d, 7a-d and 8a-d

| Compound | Zone of inhibition in mm |
|----------|-------------------------|
|          | Aspergillus niger | Aspergillus flavus | Aspergillus oryzae |
|          | 1000 | 500 | 250 | 125 | 1000 | 500 | 250 | 125 | 1000 | 500 | 250 | 125 |
| 6a       | 15   | 14  | 13  | 13  | 15   | 12  | 13  | 14  | 15   | 16  | 15  | 14  |
| 6b       | 14   | 13  | 11  | 12  | 14   | 13  | 12  | 14  | 15   | 13  | 14  | 13  |
| 6c       | 12   | 11  | 14  | 12  | 13   | 12  | 12  | 13  | 14   | 12  | 13  | 14  |
| 6d       | 13   | 14  | 14  | 13  | 13   | 13  | 14  | 13  | 14   | 11  | 11  | 12  |
| 7a       | 13   | 12  | 11  | 13  | 12   | 12  | 11  | 14  | 11   | 12  | 12  | 14  |
| 7b       | 16   | 16  | 15  | 15  | 17   | 15  | 15  | 15  | 16   | 16  | 16  | 17  |
| 7c       | 14   | 14  | 14  | 14  | 16   | 14  | 13  | 14  | 13   | 12  | 14  | 15  |
| 7d       | 14   | 12  | 13  | 13  | 13   | 14  | 14  | 13  | 13   | 12  | 12  | 13  |
| 8a       | 13   | 13  | 12  | 11  | 11   | 14  | 13  | 12  | 12   | 12  | 11  | 13  |
| 8b       | 17   | 16  | 15  | 16  | 16   | 15  | 16  | 16  | 16   | 16  | 16  | 17  |
| 8c       | 16   | 16  | 14  | 15  | 13   | 14  | 14  | 15  | 13   | 15  | 14  | 16  |
| 8d       | 12   | 14  | 14  | 14  | 14   | 13  | 14  | 15  | 12   | 11  | 13  | 14  |
| Fluconazole | 17  | 16  | 15  | 15  | 17   | 16  | 16  | 15  | 17   | 16  | 16  | 16  |

Note: Values are expressed as mean (n=3)

The antifungal activity results (Table 3) discovered that all the synthesized compounds have moderate to high antifungal activity as compared to the standard drug fluconazole. Compounds 6c-d, 7b-c and 8b-d have revealed good activity against A. niger (MTCC-281). Compound 6a-b, 7a-c and 8b-d showed good activity against A. flavus (MTCC-1782) whereas the compounds 6a, 7b-c and 8b-c have profound activity against A.
Antioxidant activities

1, 1-Diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA)

In vitro method of scavenging of the stable DPPH radical is extensively used to evaluate the antioxidant activity in less time than other methods. DPPH is a stable free radical that can accept hydrogen radical or an electron and must thus be converted to a stable diamagnetic molecule. DPPH has an odd electron and so has a strong absorption band at 517 nm. When this electron becomes paired off, the absorption decreases stoichiometrically with respect to the number of electrons or hydrogen atoms taken up. The DPPH antioxidant assay measures the hydrogen donating capacity of the molecules under study. When the free radical DPPH is reduced by the sample its color changes from violet to yellow.

The results (Fig. 1) suggested that compounds 6b, 8b and 8c showed promising RSA at all concentrations. Compound 6d, 7b, 7d and 8a was found to enhance the RSA 51.77, 56.21, 50.59 and 50.00 % respectively at Conc. 25 µg/ml. Compound 8a showed good activity i.e., 62.13 % at conc. 50 µg/ml and 64.79 at Conc. 75 µg/ml. Compound 7a and 7b showed promising activity i.e., 69.82 and 71.00 % respectively at conc. 100 µg/ml. The rest of the compounds were found to possess less to moderate activity.

Ferric ions (Fe$^{3+}$) reducing antioxidant power (FRAP)

The FRAP results (Figure 2) suggested that, the compounds 6d, 7a-d and 8a-c showed good absorbance 0.782, 0.783, 0.841, 0.811, 0.793, 0.761, 0.809 and 0.786 nm respectively at concentration 100 µg/ml, indicating that these compounds have good ferric ions (Fe$^{3+}$) reducing antioxidant power at concentrations of 100 µg/ml. In other words, these compounds showed the ability of electron donor to scavenge free radicals. The rest of the compounds showed lower absorbance as related to the standards. The higher the absorbance of the compounds indicated greater reducing power.

Figure 1: DPPH radical scavenging activity of compounds 6a-d, 7a-d and 8a-d

Figure 2: Reducing Power activity of compounds 6a-d, 7a-d and 8a-d
Ferrous (Fe$^{2+}$) metal ion chelating activity results (Figure 3) revealed that, synthesized compounds obstructed the formation of ferrous and ferrozine complex. Compounds 7b-d and 8b-d exhibited (69.15, 66.04, 69.15, 71.02, 66.04 and 68.84 % respectively) good metal chelating activity at concentration of 100 µg/ml. Highest metal chelating activity of these compounds indicates that these compounds are able to capture ferrous ion before ferrozine. This might be the reason for the higher metal chelating activity. The rest of the compounds showed reasonable to less activity when compared with the standard drugs.

CONCLUSION

The title compound of benzodiazepine derivatives attached with benzimidazole / benzothiazole and indole moieties is synthesized and characterized by using spectral and analytical data. All the compounds have been subjected for antimicrobial, antifungal and antioxidant screening. We have found that compounds are active towards antibacterial and antifungal strains. Few compounds gave better antioxidant activity compared to the standard. These studies may promote further extension of the benzodiazepine derivatives bearing benzimidazole/benzothiazole and indole moieties, which may lead to compounds with effective antioxidant and antimicrobial activities.

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