Synthesis, characterization and antibacterial activity of Cu (II) and Zn (II) complexes of 5-aminobenzofuran-2-carboxylate Schiff base ligands

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ABSTRACT
The ever-increasing spread of bacterial infection with rising antibacterial drug resistance has become a matter of global concern in the modern times. Therefore, such serious infections leading to high mortality rate has necessitated the search for new classes of effective antibacterial agents with minimum toxicity. Herein, we report the synthesis and identification of a new class of benzofuran based Schiff ligands (6a-6e) and their Cu/Zn complexes (7a-7j) via sequential reactions starting with Salicylaldehyde. Compounds 6a, 7c and 7e exhibit activity in the low microgram range against M. tuberculosis, showing the minimum inhibitory concentrations (MICs) of 1.6 µg/mL. The compounds 6e and 7b also show interesting antibacterial activity against S. Aureus, E. coli and B. Subtilis with comparable area of inhibition of standard drugs under study. This research suggests that benzofuran based compounds can serve as a promising lead scaffold in developing new drugs to combat microbial infections.

1. Introduction
The increase in drug resistance to clinically used anti-infective agents reveals that there is an urgent need of the search for new antimicrobial compounds to treat multi-resistant infections with different mechanism of action [1].

Schiff base [2] is analogous to aldehyde or ketone in which the carbonyl group (C=O) is replaced by an azomethine or imine group. The Schiff bases found number of applications as catalysts, dyes and pigments, polymer stabilizers, intermediates in synthesis, etc. [3]. The Schiff bases also exhibit a broad range of biological activities like antibacterial, antifungal, antimalarial, antituberculosis, antipyretic, anti-inflammatory and antiviral properties [4]. The imines are present in various natural and synthetic compounds. The imine group from Schiff base has been shown to be critical towards biological activities [5].

Benzofuran is a fundamental structural unit in a variety of biologically active natural products as well as synthetic materials [6]. Benzofuran derivatives shows several biological properties such as anti-inflammatory, antimicrobial, antifungal, antihyperglycemic, analgesic, antiparasitic, and antitumor activities [7–12]. Such a wide range of biological properties inherent in benzofuran scaffold justifies their extensive interest in pharmacological applications. A large number of clinically approved drugs are synthetic or naturally occurring substituted benzofuran derivatives, some of which are fused with other heterocyclic moieties [13]. In addition, substituted benzofurans find application such as of fluorescent sensor [14], oxidant [15], antioxidants, brightening agents, a variety of drugs and in other field of chemistry and agriculture [16].

Recently, it has been reported that Schiff bases and their metal complexes demonstrated significant potency against the MTB, at low micromolar level [17–19]. Numerous examples of Cu (II) and Zn (II) complexes have been explored for their significant antimicrobial activity [20].
Based on these facts, supported by literature [21], Figure 1 and in continuation of our current research interest in the field of synthesis and antimicrobial study of heterocyclic compounds [22–26], we have synthesized and screened the antimicrobial activity of series of transition metal complexes of new Schiff base ligands derived from ethyl 5-aminobenzofuran-2-carboxylate.

2. Material and methods

All required chemicals and solvents were purchased from Sigma-Aldrich (Munich, Germany) and Merck Co. (Darmstadt, Germany) and used without further purification. Melting points were determined with Fisher–Johns blocks (Fisher Scientific, Germany) and are uncorrected. The NMR spectra were recorded on a Bruker Avance 300 apparatus in DMSO-d6. The chemical shifts are measured on the $\delta$ (ppm) scale using TMS (Tetramethylsilane) as the internal standard reference. Infrared (IR) spectra measured on a FTIR-7600 Lambda Scientific Pty. Ltd. using KBr disk for the range 4000–400 cm$^{-1}$. Mass spectra obtained on BRUKER ESQUIRE HCT spectrometer. The TGA (Thermo gravimetric analysis) study carried out on Universal V4.5A TA instrument

3. Experimental

3.1. Preparation of 5-nitro salicylaldehyde (2)

The solution of salicylaldehyde (1) (1 mmol) in acetic acid (10 cm$^3$) was allowed to react with nitric acid (5 cm$^3$) at 0°C. Then reaction mixture was stirred at RT for 4 h to produce 5-nitro salicylaldehyde. The reaction mixture diluted with ice-cold water. The resulting solid was filtered and dried. White solid; Yield: 95%; m.p.: 125–127°C.

3.2. Preparation of ethyl 5-nitrobenzofuran-2-carboxylate (3)

To the solution of 5-nitro salicylaldehyde (1 mmol) in N-methyl pyrrolidine (NMP) (8 cm$^3$), Na$_2$CO$_3$ (2.5 mmol) was added stirred for 30 min., followed by addition of ethyl bromo acetate (1.5 mmol) and stirred for overnight at 100°C. The reaction mixture was dissolved in water and then extracted with ethyl acetate. The combined organic layer was washed with brine solution,
dried over Na₂SO₄ and then evaporated to dryness. Off White solid; Yield: 88%; m.p.: 176–178°C.

### 3.3. Preparation of ethyl 5-aminobenzofuran-2-carboxylate (4)

To the solution of ethyl 5-nitrobenzofuran-2-carboxylate (3) (1 mmol) in ethanol solvent under N₂ atmosphere Raney-Ni (3.0 mmol) was added to the reaction mass. Then put H₂ pressure. The reaction mixture was stirred for 6 h at room temperature. The reaction mixture was filtered through the high-flow; the combined organic layer was evaporated to dryness. Yellow solid, 91% yield, m.p.: 189–191°C; IR(KBr, υ, cm⁻¹): 3379 (-NH₂), 3309 (-NH₂), 2924 (aliphatic –CH–), 1711(C=O); ¹H-NMR (300MHz, CDCl₃): δ = 7.50 (s, 1H, Ar–H), 7.36 (d, J = 9.6 Hz, 1H, Ar–H), 6.80 (m, 2H, Ar–H), 5.08 (s, 2H, -NH₂), 4.31 (q, J = 7.5, 14.4Hz, 2H, O–CH₂–), 1.31 (m, 3H, –CH₃); ¹³C-NMR (75MHz, DMSO + CDCl₃): 157.09 (C=O), 144.04, 140.91, 140.28, 122.70, 112.11, 108.35, 106.70, 99.24, 55.79; EIMS m/z: 205.2. Found: 206.4, (M⁺ + H⁺). Anal. Calcd. for C₁₁H₁₁NO₃: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.43; H, 5.38; N, 6.80.

### 3.4. General procedure for the preparation of Schiff bases (6a–6e)

The compound (4) (0.01 mol) and appropriate aldehyde derivatives (5a–5e) (0.01 mol) taken in round bottom flask (RBF) containing 10 cm³ of methanol. Reaction mixture was refluxed for 30 min. Completion of reaction was checked with TLC. Upon cooling the reaction mixture a solid product (6a–6e) (Figure 2 and Table 1) precipitated out, which was filtered, dried and purified by recrystallization from ethanol.

#### 3.4.1. (E)-ethyl 5-(2-hydroxybenzylideneamino) benzofuran-2-carboxylate (6a)

Light green solid (EtOH); mp 130–132°C; IR(KBr, υ, cm⁻¹): 3360 (Ar–OH), 1750 (C=O), 1620 (CH=N); ¹H-NMR (DMSO-d₆, 300 MHz): δ = 12.99 (s, 1H, Ar–OH), 8.99 (s, 1H, CH=N), 7.77 (m, 3H, Ar–H), 7.62 (m, 2H, Ar–H), 7.41 (m, 1H, Ar–H), 6.95 (m, 2H, Ar–H), 4.35 (m, 2H, O–CH₂–), 1.32 (t, 3H, –CH₃); EIMS m/z: 310.32 [M⁺ + H⁺]; Anal. Calcd. for C₁₈H₁₅NO₄: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.24; H, 4.97; N, 4.65.

#### 3.4.2. (E)-ethyl 5-(5-chloro-2-hydroxybenzylideneamino) benzofuran-2-carboxylate (6b)

Pale yellow solid (EtOH); mp 162–164°C; IR(KBr, υ, cm⁻¹): 3445 (Ar–OH), 1771 (C=O), 1618 (CH=N); ¹H-NMR (DMSO-d₆, 300 MHz): δ = 12.93 (s, 1H, Ar–OH), 8.99 (s, 1H, CH=N), 7.80 (m, 4H, Ar–H), 7.62 (m, 1H, Ar–H), 7.45 (m, 1H, Ar–H), 7.01 (m, 1H, Ar–H), 6.93 (m, 2H, O–CH₂–), 1.34 (t, 3H, –CH₃); EIMS (388.21) m/z: 389.05 [M⁺ + H⁺] (100); Anal. Calcd. for C₁₈H₁₄ClNO₄: C, 55.69; H, 3.63; N, 3.61. Found: C, 55.76; H, 3.46; N, 3.58.

#### 3.4.3. (E)-ethyl 5-(5-bromo-2-hydroxybenzylideneamino) benzofuran-2-carboxylate (6c)

Light green solid (EtOH); mp 190–192°C; IR(KBr, υ, cm⁻¹): 3446 (Ar–OH), 1741 (C=O), 1624 (CH=N); ¹H-NMR (DMSO-d₆, 300 MHz): δ = 12.95 (s, 1H, Ar–OH), 9.21 (s, 1H, CH=N), 8.65 (s, 1H, Ar–H), 8.25 (m, 1H, Ar–H), 8.08 (m, 1H, Ar–H), 7.72 (m, 3H, Ar–H), 7.07 (m, 1H, Ar–H), 4.34 (m, 2H, O–CH₂–), 1.34 (t, 3H, –CH₃); EIMS (388.21) m/z: 389.05 [M⁺ + H⁺]; Anal. Calcd. for C₁₈H₁₄BrNO₄: C, 55.69; H, 3.63; N, 3.61. Found: C, 55.76; H, 3.46; N, 3.58.

#### 3.4.4. (E)-ethyl 5-(2-hydroxy-5-nitrobenzylideneamino) benzofuran-2-carboxylate (6d)

Yellow solid (EtOH); mp 162–164°C; IR(KBr, υ, cm⁻¹): 3445 (Ar–OH), 1771 (C=O), 1618 (CH=N); ¹H-NMR (DMSO-d₆, 300 MHz): δ = 12.93 (s, 1H, Ar–OH), 8.99 (s, 1H, CH=N), 7.80 (m, 4H, Ar–H), 7.62 (m, 1H, Ar–H), 7.45 (m, 1H, Ar–H), 7.01 (m, 1H, Ar–H), 6.93 (m, 2H, O–CH₂–), 1.34 (t, 3H, –CH₃); EIMS (388.21) m/z: 389.05 [M⁺ + H⁺]; Anal. Calcd. for C₁₈H₁₄BrNO₄: C, 55.69; H, 3.63; N, 3.61. Found: C, 55.76; H, 3.46; N, 3.58.

### 3.4.5. Preparation of Schiff bases (6a–6e) and metal complexes (7a–7j)

![Figure 2. Preparation of Schiff bases (6a–6e) and metal complexes (7a–7j).]
Table 1. Structures of Schiff bases (6a–6e).

| Entry | Aldehyde (5) | Schiff Base (6) | Yield (%) |
|-------|--------------|-----------------|-----------|
| a     | ![](image1)   | ![](image2)     | H         |
| b     | ![](image3)   | ![](image4)     | 84        |
| c     | ![](image5)   | ![](image6)     | 82        |
| d     | ![](image7)   | ![](image8)     | 83        |
| e     | ![](image9)   | ![](image10)    | 89        |

[M + H] (100); Anal. Calcd. for C_{18}H_{14}N_{2}O_{6}: C, 61.02; H, 3.98; N, 7.91; Found: C, 60.94; H, 4.03; N, 8.01.

3.4.5. (E)-ethyl5-((1-hydroxynaphthalen-2-yl)methyleneamino)benzofuran-2-carboxylate (6e)

Dark yellow solid (EtOH); mp 118–120°C; IR(KBr, ν, cm⁻¹): 3382 (Ar–OH), 1760 (C=O), 1625 (CH=N);¹H-NMR (DMSO-d₆, 300 MHz): δ = 15.76 (s, 1H, Ar–OH), 9.72 (s, 1H, CH=N), 8.51 (s, 1H, Ar–H), 7.97 (m, 2H, Ar–H), 7.81 (m, 4H, Ar–H), 7.54 (m, 1H, Ar–H), 7.35 (m, 1H, Ar–H), 7.05 (m, 1H, Ar–H), 4.36 (m, 2H, O–CH₂), 1.33 (m, 3H, –CH₃);¹³C-NMR (DMSO-d₆, 75 MHz) δ`: 15.76 (s, 1H, C–OH), 9.72 (s, 1H, CH=N), 8.51 (s, 1H, Ar–H), 7.97 (m, 2H, Ar–H), 7.81 (m, 4H, Ar–H), 7.54 (m, 1H, Ar–H), 7.35 (m, 1H, Ar–H), 7.05 (m, 1H, Ar–H), 4.36 (m, 2H, O–CH₂), 1.33 (m, 3H, –CH₃); EIMS m/z: 360.1 [M + H]; Anal. Calcd. for C_{22}H_{17}NO₄: C, 73.53; H, 4.77; N, 3.90; Found: C, 73.61; H, 4.86; N, 3.95.

3.5. General procedure for the preparation of metal complexes (7a–7j)

A solution of metal chloride (CuCl₂/ZnCl₂) in methanol was added gradually to a stirred ethanolic solution of the Schiff base ligand (6a–6e) in the molar ratio 1:2. The reaction mixture was further stirred for 2 h at 78°C. Then it was cooled in ice bath to ensure the complete precipitation of the formed complexes (7a–7j) Figure 2 and Table 2. The precipitated solid complex was filtered and washed with water. Finally, the complex was washed with diethyl ether and dried in vacuum desiccators over anhydrous CaCl₂.

3.5.1. Cu (II) complex (7a)

IR(KBr, ν, cm⁻¹): 3430, 1751, 1530, 1410, 520, 420.

3.5.2. Cu (II) complex (7b)

IR(KBr, ν, cm⁻¹): 3430, 1751, 1530, 1410, 520, 420.

3.5.3. Cu (II) complex (7c)

IR(KBr, ν, cm⁻¹): 3440, 1761, 1615, 1422, 530, 425.; EIMS m/z [M + 2]: 835.17

3.5.4. Cu (II) complex (7d)

IR(KBr, ν, cm⁻¹): 3430, 1750, 1620, 1420, 520, 430.

3.5.5. Cu (II) complex of (7e)

IR(KBr, ν, cm⁻¹): 3440, 1761, 1615, 1422, 530, 425.; EIMS m/z [M + 2]: 835.17

3.5.6. Zn (II) complex (7f)

IR(KBr, ν, cm⁻¹): 3393, 3108, 1752, 1604, 1589, 1459, 1435, 536, 454.

3.5.7. Zn (II) complex (7g)

IR(KBr, ν, cm⁻¹): 3422, 1769, 1619, 1599, 1451, 1406, 537, 486, 457.
Table 2. Structures of metal complexes (7a–7j).

| Entry | Complex | Colour | Entry | Complex | Colour |
|-------|---------|--------|-------|---------|--------|
| 7a    | Green   |        | 7f    | Yellow  |        |
| 7b    | Green   |        | 7g    | Yellow  |        |
| 7c    | Green   |        | 7h    | Yellow  |        |
| 7d    | Green   |        | 7i    | Yellow  |        |
| 7e    | Green   |        | 7j    | Yellow  |        |

3.5.8. Zn (II) complex (7h)
IR(KBr, υ, cm⁻¹): 3421, 3104, 1770, 1605, 1589, 1452, 1407, 535, 527, 485, 447 cm⁻¹; ¹H-NMR (DMSO-d₆, 300 MHz): δ = 9.29 (s, 2H), 7.84 (m, 2H), 7.69 (m, 2H), 7.60 (s, 2H), 7.52 (s, 2H), 7.46 (m, 2H), 7.28 (m, 2H), 6.72 (m, 2H), 4.36 (m, 4H), 1.34 (t, 6H); EIMS m/z: 876.2 [M+1].

3.5.9. Zn (II) complex (7i)
IR(KBr, υ, cm⁻¹): 3403, 1752, 1619, 1608, 1473, 1449, 527, 450, 436.

3.5.10. Zn (II) complex (7j)
IR(KBr, υ, cm⁻¹): 3470, 3439, 1762, 1617, 1601, 1459, 1426, 536, 463, 453; EIMS m/z [M+1]: 819.1.

4. Results and discussion
4.1. Chemistry

The main purpose of this work was the synthesis, identification and in vitro antimicrobial screening of newer Schiff bases along with their Cu (II) and Zn
The 13C NMR of Schiff base 6b has 18 carbon resonances. The spectrum has shown characteristic signals at 158.45 and 158.750 ppm are assigned to azomethine and carbonyl carbons respectively. Aromatic carbons have resonated in the expected region of 112.98–146.19 ppm. The peak at 61.29 and 14.07 ppm are assigned to methylene carbon (O–CH2–) and methyl carbon (–CH3) respectively.

The FTIR spectrum of the Schiff base 6b shows a broad band at 3445 cm−1, assigned to ν(OH) of the phenolic group. This band has disappeared in all the complexes indicating the coordination of phenolic oxygen via de-protonation. This fact is even confirmed by the shift of phenolic (C−O) vibrations in the ligand, from 1413 cm−1 to higher frequencies in all the complexes. However, the complexes have shown new broad peaks in the region of 3393–3447 cm−1, assignable to coordinated water. The vibrations at 1769 cm−1 and 1619 cm−1 in the ligand are due to ester carbonyl ν(C=O) and imine ν(C=N) respectively. The imine ν(C=N) vibrations have shifted to lower frequencies in all the complexes, indicating the participation of phenolic oxygen and imine nitrogen in the coordination. The key IR absorption bands are summarized in Table 3.

The thermal behaviour of some selected metal complexes was characterized on the basis of TGA method. The thermal behaviour of the metal complexes was studied in temperature range of 25–1000°C. The Cu (II) complex 7a decomposed in four steps. The first step occurred below 100°C and corresponded to the loss of water molecules of Lattice water. The second step of decomposition appeared within the temperature range 110–160°C and corresponded to the loss of coordinated water molecules. The organic ligand was further decomposed within the temperature range 400°C leaving behind CuO as final product. This pattern of observation of TGA found similar for other complexes including Zn (II) complexes. The plateau observed for Zn (II) complexes above the 400°C is due to formation of stable ZnO. The molar conductivity values were

### Table 3. Spectral data of Schiff bases (6a–6e) and metal complexes (7a–7j).

| Sr. No. | Entry | Phenolic ν(–OH) | Lattice water ν(–OH) | Ester ν(C=O) | Imine ν(C=N) | Water ν(OH) | O-H/N | Phenic ν(C=O) | Water ν(OH) | % Metal | M. cond. Δm (Ω−1 mol−1 cm2) |
|---------|-------|-----------------|----------------------|-------------|-------------|-------------|-------|--------------|-------------|--------|----------------------------|
| 01      | 6a    | 3360            | –                    | 1750        | 1620        | 1408        | –     | –            | –           | –      | –                          |
| 02      | 6b    | 3445            | –                    | 1771        | 1618        | 1413        | –     | –            | –           | –      | –                          |
| 03      | 6c    | 3421            | –                    | 1791        | 1619        | 1409        | –     | –            | –           | –      | –                          |
| 04      | 6d    | 3446            | –                    | 1790        | 1624        | 1418        | –     | –            | –           | –      | –                          |
| 05      | 6e    | 3382            | –                    | 1760        | 1625        | 1421        | –     | 9.7          | 15.76      | –      | –                          |
| 06      | 7a    | 3430            | –                    | 1751        | 1624        | 1440        | 520   | 420          | –           | 8.90   | 8.87 (17.2)                |
| 07      | 7b    | 3421            | –                    | 1769        | 1620        | 1430        | 530   | 430          | –           | 8.20   | 8.09 (11.6)                |
| 08      | 7c    | 3447            | –                    | 1773        | 1608        | 1453        | 522   | 440          | –           | 7.25   | 7.27 (9.7)                 |
| 09      | 7d    | 3430            | –                    | 1750        | 1620        | 1436        | 520   | 430          | –           | 7.90   | 7.88 (10.2)                |
| 10      | 7e    | 3440            | –                    | 1761        | 1615        | 1442        | 530   | 425          | –           | 7.69   | 7.78 (13.5)                |
| 11      | 7f    | 3393            | –                    | 1752        | 1604        | 1451        | 536   | 454          | –           | 9.14   | 9.11 (14.3)                |
| 12      | 7g    | 3422            | –                    | 1769        | 1619        | 1451        | 537   | 457          | 9.29        | 8.30   | 8.31 (9.6)                 |
| 13      | 7h    | 3421            | –                    | 1770        | 1605        | 1452        | 535   | 447          | –           | 7.58   | 7.47 (10.7)                |
| 14      | 7i    | 3403            | –                    | 1752        | 1608        | 1449        | 527   | 450          | –           | 8.15   | 8.09 (16.2)                |
| 15      | 7j    | 3439            | –                    | 1762        | 1601        | 1459        | 536   | 453          | –           | 8.08   | 7.99 (11.3)                |
Table 4. ESR spectral data of Cu (II) complexes.

| COMP in PCS-RT | g_∥ value | g_⊥ value | g_avg | G      |
|----------------|-----------|-----------|-------|--------|
| 7c             | 2.3242    | 2.066     | 2.152 | 5.053  |
| 7d             | 2.2915    | 2.066     | 2.141 | 4.540  |
| 7e             | 2.3665    | 2.066     | 2.166 | 5.717  |

measured at room temperature in DMF (10^{-3} M) for all the complexes. The values obtained fall in the range of 8.48–20.2 indicating non-electrolytic nature of the complexes [27]. The molar conductivity data is represented in Table 3.

The ESR spectrum of the Cu (II) complex in a polycrystalline state was recorded at room temperature. The g_∥ and g_⊥ values for 7c, 7d and 7e are reported in the Table 4. The g_avg value is calculated and reported in the same table. The spectrum showed asymmetric bands with two g values. The values are almost same for all complexes indicating that the type of bonding is the same in all complexes and that the Cu-O bond lengths do not vary much from complex to complex [28,29].

The trend g_∥ > g_⊥ > 2.00277, indicates that the unpaired electron lay predominately in the d_{x^2−y^2} orbital with possibly mixing of d_{z^2} orbital because of the low symmetry.

The axial symmetry parameter “G” is determined as

\[ G = \frac{(g_∥ - 2.00277)}{(g_⊥ - 2.00277)} \]

G values found to be more than 4 suggesting very weak or no interaction in the solid state.

The results of elemental analyses and spectral characterization of the prepared Schiff bases and their metal complexes are in satisfactory agreement with the theoretical values which confirm the proposed molecular formula of these compounds as represented in Tables 1 and 2.

5. Microbiology

5.1. In vitro antitubercular assay

The anti-tubercular activity of synthesized compounds was evaluated using previously reported method Almar Blue assay (MABA) [30]. A blue colour in the well was interpreted as no bacterial growth, and pink colour was scored as growth. From this experiment, MIC (minimum inhibitory concentration) can be defined as lowest drug concentration which prevented the colour change from blue to pink. The observed results are represented in Table 5 and Figure 3.

The hydroxyl fatty acids like Mycolic acids present in the mycobacterial cell wall are significant key structure for survival and growth of M. tuberculosis bacteria. Majority of first line drugs against M. tuberculosis works by inhibiting biosynthesis of mycolic acids leading to mycobacterial cell death. Recent advancements revealed Schiff bases derivatives as more potent compound against M. tuberculosis H37 RV strain with minimum MIC value. Enticed by these reports, all synthesized compounds were evaluated against M. tuberculosis (H37 RV strain ATCC No- 27294) by Microplate Alamar Blue Assay (MABA). All compounds exhibited moderate to good antitubercular activity as compared to standard drugs. At 1.60 μg/mL concentration compounds 6a, 7c and 7e showed inhibitory activity against M. tuberculosis.

5.2. In vitro antibacterial assay

The test compounds were screened in vitro for antibacterial activity against S. Aureus, E. coli and B. Subtilis. The effect of test compounds on the several bacterial strains were assayed by Disc diffusion method. The compounds are allowed to diffuse out into the medium and interact in a plate freshly seeded with the test organisms. The resulting zones of inhibition shall be uniformly circular as there will be a confluent lawn of growth. The diameter of zone of inhibition can be measured in cm.

Petriplates containing 20 mL Muller Hinton medium were seeded with 24 h culture of bacterial strains. The
Table 6. Antibacterial activity of Schiff bases (6a–6e) and metal complexes (7a–7j) with Area of Inhibition (cm).

| Sr. No. | Compounds | S. Aureus 200 μg/mL | S. Aureus 100 μg/mL | E. Coli 200 μg/mL | E. Coli 100 μg/mL | B. Subtilis 200 μg/mL | B. Subtilis 100 μg/mL |
|---------|-----------|---------------------|---------------------|------------------|------------------|----------------------|----------------------|
| 1.      | 6a        | 1.10                | 0.95               | 1.20             | 1.00             | 1.00                 | 0.90                 |
| 2.      | 6b        | 1.20                | 1.00               | 1.10             | 1.00             | 1.10                 | 0.90                 |
| 3.      | 6c        | 1.10                | 1.00               | 1.20             | 1.00             | 1.20                 | 1.00                 |
| 4.      | 6d        | 1.20                | 1.00               | 0.95             | 0.80             | 0.95                 | 0.85                 |
| 5.      | 6e        | 0.90                | 0.70               | 0.80             | 0.70             | 1.00                 | 0.90                 |
| 6.      | 7a        | 1.20                | 1.00               | 0.95             | 0.80             | 0.95                 | 0.85                 |
| 7.      | 7b        | 0.90                | 0.90               | 0.95             | 0.90             | 0.90                 | 0.80                 |
| 8.      | 7c        | 0.95                | 0.85               | 0.95             | 0.90             | 1.00                 | 0.90                 |
| 9.      | 7d        | 1.00                | 0.80               | 1.00             | 0.90             | 0.90                 | 0.85                 |
| 10.     | 7e        | 1.00                | 0.90               | 0.85             | 0.80             | 0.85                 | 0.75                 |
| 11.     | 7f        | 1.50                | 1.20               | 1.00             | 0.90             | 0.95                 | 0.90                 |
| 12.     | 7g        | 0.90                | 0.90               | 1.10             | 0.90             | 1.20                 | 0.90                 |
| 13.     | 7h        | 1.00                | 0.80               | 1.20             | 1.00             | 1.00                 | 0.90                 |
| 14.     | 7i        | 0.95                | 0.85               | 1.20             | 1.10             | 1.20                 | 1.00                 |
| 15.     | 7j        | 1.10                | 1.00               | 1.50             | 1.50             | 1.30                 | 1.10                 |
| 16.     | Penicillin| 2.00                | –                  | 0.80             | –                | 1.00                 | –                    |
| 17.     | Streptomycin| 0.70                | –                  | 0.70             | –                | 3.00                 | –                    |

Figure 4. Antibacterial activity at concentration 100 μg/mL.

In this paper, we synthesized and characterized some new Schiff bases derivatives with benzo[1,2-b:4,5-b’]dithiolane core and their Cu (II) & Zn (II) complexes in good yields. Followed by evaluation of their antibacterial activity against a panel of bacterial strains. The observed antimicrobial screening results indicate that some of the newly obtained compounds showed significant antibacterial activity, especially against M. tuberculosis. Among them, the activities of compounds 6a, 7c and 7e were strong against M. tuberculosis which is almost two fold higher than that of Pyrazinamide and Ciprofloxacin. In addition to this compounds 6e and 7b have shown to exhibit promising antimicrobial activity against S. aureus, E. coli and B. subtilis.

6. Conclusion

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Disclosure statement

No potential conflict of interest was reported by the authors.
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