Design, Synthesis and Biological Screening of New BenzimidazoleDerivatives

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Abstract. In this study, we synthesized a series of benzimidazole compounds containing 1,3,4-thiadiazole ring from many reaction steps. The obtained benzimidazole series were characterized by melting point, Data from FT-IR and 1H-13C-NMR and In vitro screening of antibacterial activity against strains of selected pathogenic Gram-positive (Staphylococcus aureus, Bacillus subtilis) and Gram-negative (Acinetobacter baumannii, Pseudomonas aeruginosa) bacteria relative to (Amoxicillin) and (Ciprofloxacin) as standard antibacterial agents has shown high pharmacological activity.

Keywords: benzimidazole, 1,3,4-thiadiazole, antibacterial activity, 1,2-phenylenediamine

1. Introduction

Benzimidazoles remain one of the most robust classes of antimicrobial agents, despite several attempts to create a new structural template in the search for more effective antimicrobials. [1–8]. Benzimidazoles are considered to be a possible class of heterocyclic bioactive compounds with a wide range of biological activities. In fact, this nucleus is a component of vitamin B12 [9]. As a consequence, benzimidazoles have diverse biological properties, such as antifungal,[4], antitumor[10–12], antiviral[13,14], antihistaminic[15], benzimidazole and its derivatives have also been used as optical lasers and polymer dyes in optoelectronics.[16,17], For the identification of biologically important molecules such as DNA, RNA or proteins and enzymes, organic luminophores, fluorescent fags [18]. In a large spectrum of therapeutically important agents, The nucleus of 1,3,4-thiadiazole has been incorporated. Which mainly provides antimicrobial operations [19]. In many fields, there are enough applications for 1,3,4-thiadiazole. As antibacterial medicines, the first applications of the medicinal industry were [20].

2. Experimental

2.1. Materials and physical measurements

Without purification from Aldrich, many of the starting materials and solvents were collected and used. On the SHIMADZU model FT-IR-8400S, the FT-IR spectrum was registered, 1H and 13C-NMR spectra were recorded on the BRUKER model Ultra Shield 500 MHz spectrophotometer using DMSO-d6 as solvent and TMS as internal comparison. The melting points were registered and are unreliable by the Stuart smp3 electronic system.
2.2. Methods of preparation and physical data of synthesised compounds 1(a,b), 2(a–e), 3(a–e), and 4(a–j).

2.2.1. Common method for synthesising 1(a-b) of compounds.
Mixing (20) mmol of o-phenylene diamine derivatives, (20 mmol) of CS₂, (20) mmol of KOH, (25) mL of EtOH and (5) mL of reflux-heated H₂O in a 100 ml circular flask for 3 hours, carefully inserted (0.5 g) of charcoal and continued reflux for 10 minutes, Filtered charcoal was extracted by filtration and (25 mL) of hot water was added. In order to complete the crystallization, the mixture obtained was held in an ice bath for (3 h), the material obtained was distilled, dried and recrystallized from ethanol, and TLC (mobile phase: CH₃(CH₂)₄CH₃: CH₃COOCH₂CH₃ (1:1))

2.2.1.1. 2-mercaptobenzimidazole (1a).
Light beige powder, m.p 305-307 °c, FT-ir (cm⁻¹) 3155 (NH), 3093 (CH, aromatic), 2569 (S-H), 1620 (C=N), 1585 and 1462 (C=C, aromatic) was obtained.

2.2.1.2. 2-mercapto-5-methylbenzimidazole (1b).
Light brown powder, yield (80%), m.p 286-288 °C, FT-ir (cm⁻¹) 3132 (N-H), 3041 (C-H, aromatic), 2968-2862 (C-H, aliphatic), 2573 (S-H), 1625 (S-H), 1625 (C=N), 1593 and 1469 (C=C, aromatic) was obtained.

2.2.2. Specific protocol for compound synthesis 2(a-e).
For 3 hours, The resultant mixture of (ArCOOH) (20 mmol), (NH₂NHCSNH₂) (1.82 g, 20 mmol) and POCl₃ (10 mL) was refluxed gently. H₂O (50 mL) was applied slowly after cooling and The mixture of reactions was refluxed and purified for 4 h. The distilled KOH solution neutralized the solvent and the precipitate was purified and recycled from EtOH, and TLC was tested for the completion of the reaction and for the purity of the compounds (mobile phase: CH₃(CH₂)₄CH₃: CH₃COOCH₂CH₃(1:3)).

2.2.2.1. 2-Amino-5-(phenyl)-1,3,4-thiadiazole (2a).
Pale yellow powder, yield (76%), m.p 224-227 °C, FT- ir (cm⁻¹) 3275 and 3113 (NH₂), 3043 (C-H, aromatic), 1631 (C=N), 1581 and 1469 (C=C, aromatic) was obtained.

2.2.2.2. 2-Amino-5-(4-chlorophenyl)-1,3,4-thiadiazole (2b).
Yellow powder, yield (80%), m.p 226-229 °C, FT- ir (cm⁻¹) 3271 and 3105 (NH₂), 3047 (C-H, aromatic), 1631 (C=N), 1597 and 1462 (C=C, aromatic) was obtained.

2.2.2.3. 2-Amino-5-(2-chlorophenyl)-1,3,4-thiadiazole (2c).
Yellow powder, yield (70%), m.p 214-216 °C, Rf = 0.58; FT- ir (cm⁻¹) 3282 and 3105 (NH₂), 3028 (C-H, aromatic), 1635 (C=N), 1597 and 1458 (C=C, aromatic) was obtained.

2.2.2.4. 2-Amino-5-(4-nitrophenyl)-1,3,4-thiadiazole (2d).
Dark yellow powder, yield (78%), m.p 244-247 °C, FT- ir (cm⁻¹) 3259 and 3113 (NH₂), 3066 (C-H, aromatic), 1627 (C=N), 1597 and 1458 (C=C, aromatic), 1508 and 1346 (NO₂) was obtained.

2.2.2.5. 2-Amino-5-(3,5-dinitrophenyl)-1,3,4-thiadiazole (2e).
Dark yellow powder, yield (75%), m.p 265-268 °C, FT- ir (cm⁻¹) 3275 and 3116 (NH₂), 3055 (C-H, aromatic), 1624 (C=N), 1593 and 1419 (C=C, aromatic), 1539 and 1350 (NO₂) was obtained.

2.2.3. Common method for synthesizing 3(a–e) compounds.
Compounds 2(a-e) (5 mmol) were dissolved in DMF, and the reaction mixtures were added to TEA (5 mmol). The reaction mixtures were slowly applied to chloroacetyl chloride (10 mmol). The mixture of reactions was
heated under reflux for 2 h. The solution was then applied to crushed ice, filtering the substance collected, washed with H2O, dried and recrystallized from C2H5OH.

2.2.3.1. 2-chloro-N-(5-phenyl-1,3,4-thiadiazol-2-yl)acetamide (3a)
Pale yellow powder, yield (82%), m.p 233-235 °C, FT-ir (cm⁻¹) 3182 (N-H), 3043 (C-H, aromatic), 2947, 2835 (C-H, aliphatic), 1705 (C=O), 1627 (C=N), 1573 and 1438 (C=C, aromatic) was obtained.

2.2.3.2. 2-chloro-N-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (3b)
Beige powder, yield (85%), m.p 254-256 °C, FT-ir (cm⁻¹) 3170 (N-H), 3032 (C-H, aromatic), 2939, 2831 (C-H, aliphatic), 1705 (C=O), 1631 (C=N), 1570 and 1442 (C=C, aromatic) was obtained.

2.2.3.3. 2-chloro-N-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (3c)
Beige powder, yield (84%), m.p 230-232 °C, FT-ir (cm⁻¹) 3174 (N-H), 3032 (C-H, aromatic), 2939, 2839 (C-H, aliphatic), 1708 (C=O), 1624 (C=N), 1581 and 1438 (C=C, aromatic) was obtained.

2.2.3.4. 2-chloro-N-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (3d)
Dark beige powder, yield (80%), m.p 250-252 °C, Rf = 0.47; FT-ir (cm⁻¹) 3163 (N-H), 3032 (C-H, aromatic), 2943, 2839 (C-H, aliphatic), 1708 (C=O), 1627 (C=N), 1593 and 1438 (C=C, aromatic), 1519 and 1346 (NO2) was obtained.

2.2.3.5. 2-chloro-N-(5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (3e)
Pale brown powder, yield (86%), m.p 240-243 °C, FT-ir (cm⁻¹) 3182 (N-H), 3035 (C-H, aromatic), 2943, 2877 (C-H, aliphatic), 1712 (C=O), 1624 (C=N), 1593 and 1438 (C=C, aromatic), 1543 and 1350 (NO2) was obtained.

2.2.4. The general protocol for compound synthesis 4(a-j).
A mixture of 2-chloro-N- (5-((un)substituted phenyl)-1,3,4 thiadiazole-2-yl) acetamide (5 mmol), compounds 1(a,b) (5 mmol) and K2CO3 (5 mmol) in DMF (25 mL) was refluxed for 10 h. The solvent was then added into the crushed ice, refining and recrystallizing the liquid derived from ethanol, TLC tested the end of the reaction and the compounds' purity. (mobile phase: CH3(CH2)4CH3: CH3COOCH2CH3 (2:3)).

2.2.4.1. 2-((benzimidazol-2-yl)thio)-N-(5-phenyl-1,3,4-thiadiazol-2-yl)acetamide (4a)
Beige powder, yield (60%), m.p 188-190 °C, FT-ir (cm⁻¹) 3336 (N-H), 3155 (N-H, benzimidazole),3035 (C-H, aromatic), 2951, 2881 (C-H, aliphatic), 1670 (C=O), 1616 (C=N), 1558 and 1435 (C=C, aromatic); 1H-NMR (DMSO-d6, 500 MHz, δ) 4.45 (s, 2H, CH2), 7.15-7.75 (m, 9H, Ar-H), 8.58 (s, 1H, NH), 12.55 (s, 1H, benzimidazole-NH); 13C-NMR (DMSO-d6, 125 MHz, δ) 36.74, 114.35, 121.88, 122.97, 127.08, 129.66, 130.42, 131.47, 139.97, 150.62, 161.08, 162.57, 169.43 was obtained.

2.2.4.2. 2-((5-methylbenzimidazol-2-yl)thio)-N-(5-phenyl-1,3,4-thiadiazol-2-yl)acetamide (4b)
Dark brown powder, yield (71%), m.p 222-225 °C, FT-ir (cm⁻¹) 3317 (N-H), 3167 (N-H, benzimidazole),3028 (C-H, aromatic), 2908, 2808 (C-H, aliphatic), 1674 (C=O), 1627 (C=N), 1570 and 1438 (C=C, aromatic); 1H-NMR (DMSO-d6, 500 MHz, δ) 4.45 (s, 2H, CH2), 7.35-7.75 (m, 9H, Ar-H), 8.58 (s, 1H, NH), 12.55 (s, 1H, benzimidazole-NH); 13C-NMR (DMSO-d6, 125 MHz, δ) 36.74, 114.35, 121.88, 122.97, 127.08, 129.66, 130.42, 131.47, 139.97, 150.62, 161.08, 162.57, 169.43 was obtained.

2.2.4.3. 2-((benzimidazol-2-yl)thio)-N-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4c)
Dark brown powder, yield (71%), m.p 222-225 °C, FT-ir (cm⁻¹) 3317 (N-H), 3167 (N-H, benzimidazole),3028 (C-H, aromatic), 2908, 2808 (C-H, aliphatic), 1674 (C=O), 1627 (C=N), 1570 and 1438 (C=C, aromatic); 1H-NMR (DMSO-d6, 500 MHz, δ) 2.37 (s, 3H, CH3), 4.43 (s, 2H, CH2), 6.95-7.52 (m, 8H, Ar-H), 8.59 (s, 1H, NH), 13.14 (s, 1H, benzimidazole-NH); 13C-NMR (DMSO-d6, 125 MHz, δ) 36.74, 114.35, 121.88, 122.97, 127.08, 129.66, 130.42, 131.47, 139.97, 150.62, 161.08, 162.57, 169.43 was obtained.

2.2.4.4. 2-((benzimidazol-2-yl)thio)-N-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4e)
Dark brown powder, yield (62%), m.p 190-192 °C, FT-ir (cm⁻¹) 3298 (N-H), 3163 (N-H, benzimidazole),3051 (C-H, aromatic), 2900, 2819 (C-H, aliphatic), 1678 (C=O), 1620 (C=N), 1593 and 1438 (C=C, aromatic); 1H-
NMR (DMSO-d$_6$, 500 MHz, δ) 4.34 (s, 2H, CH$_2$), 7.12-7.91 (m, 8H, Ar-H), 8.55 (s, 1H, NH), 12.60 (s, 1H, benzimidazole-NH); $^{13}$C-NMR (DMSO-d$_6$, 125 MHz, δ) 35.40, 119.71, 122.71, 128.29, 129.77, 130.27, 132.70, 134.40, 135.63, 149.68, 159.01, 162.73, 169.30 was obtained.

2.2.4.4. 2-((5-methylbenzimidazol-2-yl)thio)-N-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4d)

Dark beige powder, yield (58%), m.p 190-194 °C, FT-IR (cm$^{-1}$) 3305 (N-H), 3159 (N-H, benzimidazole), 3047 (C-H, aromatic), 2939, 2873 (C-H, aliphatic), 1678 (C=O), 1624 (C=N), 1593 and 1438 (C=C, aromatic) was obtained.

2.2.4.5. 2-((benzimidazol-2-yl)thio)-N-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4e)

Dark beige powder, yield (68%), m.p 217-219 °C, FT-IR (KBr disk, cm$^{-1}$) 3325 (N-H), 3155 (N-H, benzimidazole), 3035 (C-H, aromatic), 2962, 2897 (C-H, aliphatic), 1674 (C=O), 1620 (C=N), 1573 and 1435 (C=C, aromatic); $^1$H-NMR (DMSO-d$_6$, 125 MHz, δ) 36.31, 114.35, 121.91, 128.17, 130.02, 131.18, 131.40, 131.80, 139.94, 150.36, 157.45, 163.26, 169.06 was obtained.

2.2.4.6. 2-((5-methylbenzimidazol-2-yl)thio)-N-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4f).

Pale brown powder, yield (55%), m.p 225-227 °C, FT-IR (cm$^{-1}$) 3282 (N-H), 3167 (N-H, benzimidazole), 3032 (C-H, aromatic), 2920, 2823 (C-H, aliphatic), 1678 (C=O), 1624 (C=N), 1577 and 1435 (C=C, aromatic); $^1$H-NMR (DMSO-d$_6$, 125 MHz, δ) 2.36 (s, 3H, CH$_3$), 4.42 (s, 2H, CH$_2$), 6.94-7.62 (m, 7H, Ar-H), 8.53 (s, 1H, NH), 12.47 (s, 1H, benzimidazole-NH); $^{13}$C-NMR (DMSO-d$_6$, 125 MHz, δ) 36.31, 114.35, 121.91, 128.17, 129.42, 130.98, 131.23, 131.48, 132.16, 149.14, 150.36, 157.45, 163.26, 169.06 was obtained.

2.2.4.7. 2-((benzimidazol-2-yl)thio)-N-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4g).

Brown powder, yield (59%), m.p 193-196 °C, FT-IR (cm$^{-1}$) 3317 (N-H), 3155 (N-H, benzimidazole), 3074 (C-H, aromatic), 2935, 2866 (C-H, aliphatic), 1670 (C=O), 1624 (C=N), 1589 and 1431 (C=C, aromatic), 1516, 1342 (NO$_2$) was obtained.

2.2.4.8. 2-((5-methylbenzimidazol-2-yl)thio)-N-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4h).

Dark brown powder, yield (63%), m.p 189-192 °C, FT-IR (KBr disk, cm$^{-1}$) 3329 (N-H), 3155 (N-H, benzimidazole), 3074 (C-H, aromatic), 2927, 2862 (C-H, aliphatic), 1681 (C=O), 1627 (C=N), 1593 and 1435 (C=C, aromatic), 1523, 1546 (NO$_2$) was obtained.

2.2.4.9. 2-((benzimidazol-2-yl)thio)-N-(5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4i).

Dark brown powder, yield (66%), m.p 246-249 °C, FT-IR (KBr disk, cm$^{-1}$) 3321 (N-H), 3174 (N-H, benzimidazole), 3089 (C-H, aromatic), 2981, 2885 (C-H, aliphatic), 1685 (C=O), 1631 (C=N), 1589 and 1423 (C=C, aromatic), 1539 and 1346 (NO$_2$) was obtained.

2.2.4.10. 2-((5-methylbenzimidazol-2-yl)thio)-N-(5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl)acetamide (4j).

Dark brown powder, yield (60%), m.p 215-218 °C, FT-IR (cm$^{-1}$) 3348 (N-H), 3167 (N-H, benzimidazole), 3101 (C-H, aromatic), 2951, 2873 (C-H, aliphatic), 1662 (C=O), 1624 (C=N), 1589 and 1423 (C=C, aromatic), 1543 and 1346 (NO$_2$); $^1$H-NMR (DMSO-d$_6$, 500 MHz, δ) 2.31 (s, 3H, CH$_3$), 4.52 (s, 2H, CH$_2$), 6.93-7.76 (m, 6H, Ar-H), 8.61 (s, 1H, NH), 12.47 (s, 1H, benzimidazole-NH); $^{13}$C-NMR (DMSO-d$_6$, 125 MHz, δ) 21.38, 36.23, 123.59, 125.94, 126.19, 128.52, 130.60, 132.06, 132.87, 136.05, 148.70, 159.16, 162.74, 168.17 was obtained.
3. Results and discussion

3.1. Synthesis

The synthetic route of title compounds 4(a-j) is presented in Scheme 1. Cyclization of 5-(un)-substituted-o-phenylenediamine with CS₂. The compounds 1(a, b) were given in the existence of KOH in the EtOH medium. These synthesized compounds were characterized by FT-IR. In the IR spectra of the compounds, stretching band belonging to (N-H), (S-H) and (C=N) were observed at the range (3155-3132 cm⁻¹), (2573-2569 cm⁻¹) and (1625-1620 cm⁻¹) respectively.

In the presence of phosphorous oxide chloride, 2-amino-5-(substituted)-1,3,4-thiadiazole 2(a-e) was synthesized by the reaction of different carboxylic acid derivatives with thiosemicarbazide. Compound 2(a-e) FT-IR spectra demonstrated the presence at (1635-1624 cm⁻¹) of a group of C = N and two bands at (3282-3259 cm⁻¹) and (3116-3105 cm⁻¹) that may be attributed to asymmetric and symmetric stretching vibrations of the NH₂ group.

Compounds 3(a-e) were synthesized by a reaction of compounds 2(a-e) with chloroacetyl chloride in the presence of TEA in the DMF medium to yielded compounds 3(a-e). The chemical structures of these compounds were elucidated via FT-IR. In the IR spectra of all compounds, the occurrence of amide group (N-H) bonds was confirmed through bands in the region of (3182-3163 cm⁻¹). Due to the occurrence of a sharp peak at (1712-1705 cm⁻¹), the inclusion of the carbonyl group (C = O) in the structure is confirmed. Also confirmed by the existence of a sharp absorption band at (1631-1624 cm⁻¹) was the existence of C = N in the 1,3,4-thiadiazole nucleus. Compounds 1(a, b) were reacted with compounds (3a-e) in the DMF medium in the anhydrous K₂CO₃ to give the target compounds 4(a-j) in the final step. FT-IR, 1H NMR, and 13C identified the chemical structures of all target compounds. The IR data acquired for the final compounds 4(a-j) allow us to a large degree to validate their formation. By analyzing data for both synthesized compounds and absorption peaks at (3488-3282 cm⁻¹), (3174-3155 cm⁻¹) and (1685-1662 cm⁻¹) the presence of N-H amide, N-H benzimidazole and C=O groups was confirmed, respectively. The presence of C-H bonds in the final products was allocated to a steep peak at (2981-2808 cm⁻¹). Sharp absorption band at (1631-1616) confirmed the presence of C=N in the benzimidazole and 1,3,4-thiadiazole nucleus. In the ¹H NMR spectra of all compounds, the methylene protons have resonated at δ (4.52-4.34) ppm and this down filed value can be attributed to the inductive effect of the carbonyl group. The singlet NH signal of benzimidazole has appeared at δ (13.14-12.38) in all compounds. The signals belonging to the aromatic region was seen at δ (7.91-6.93) ppm. In the ¹³C NMR spectra, the methylene carbon between the sulfur atom and carbonyl group was observed at δ (36.74-35.33) ppm. Two carbons on the thiadiazole ring were observed at δ (163.26-157.45) ppm. While the carbonyl carbon was observed at δ (169.43-167.55) ppm. All other aromatic carbons were recorded between δ (139.97) and δ (114.35).
Scheme 1. General scheme of the prepared compounds

Table 1. Physical properties of molecules that are synthesized

| Comp. No. | R | R₁ | Molecular Formula | M.wt | Color     | M.P (°C) | Yield % | Rf   |
|-----------|---|----|-------------------|------|-----------|----------|---------|------|
| 1a        | H |     | C₈H₇N₂S          | 150.20 | Light beige | 305-307 | 78      | 0.57 |
| 1b        | CH₃ |     | C₈H₈N₂S         | 164.23 | Light brown | 286-288 | 80      | 0.59 |
| 2a        | H |     | C₈H₇N₂S         | 177.23 | Pale yellow | 224-227 | 76      | 0.46 |
| 2b        | 4-Cl |     | C₈H₇ClN₂S      | 211.67 | Yellow     | 226-229 | 80      | 0.51 |
| 2c        | 2-Cl |     | C₈H₇ClN₂S      | 211.67 | Yellow     | 214-216 | 70      | 0.58 |
| 2d        | 4-NO₂ |     | C₈H₆N₂O₂S      | 222.22 | Dark yellow | 244-247 | 78      | 0.45 |
| 2e        | 3,5-diNO₂ | | C₈H₆N₂O₂S | 267.22 | Dark yellow | 265-268 | 75      | 0.62 |
| 3a        | H |     | C₁₀H₇ClN₂O₂S   | 253.70 | Pale yellow | 233-235 | 82      | 0.48 |
| 3b        | 4-Cl |     | C₁₀H₈ClN₂O₂S   | 288.15 | Beige     | 254-256 | 85      | 0.54 |
| 3c        | 2-Cl |     | C₁₀H₇ClN₂O₂S   | 288.15 | Beige     | 230-232 | 84      | 0.48 |
| 3d        | 4-NO₂ |     | C₁₀H₈ClN₂O₂S   | 298.70 | Dark beige | 250-252 | 80      | 0.47 |
| 3e        | 3,5-diNO₂ | | C₁₀H₇ClN₂O₂S | 343.70 | Pale yellow | 240-243 | 86      | 0.53 |
| 4a        | H |     | C₁₀H₇N₂O₂S₂     | 367.45 | Beige     | 188-190 | 60      | 0.43 |
| 4b        | CH₃ |     | C₁₀H₈N₂O₂S₂   | 381.47 | Dark brown | 222-225 | 71      | 0.46 |
| 4c        | H | 4-Cl | C₁₁H₁₂Cl₅N₂O₅S₂ | 401.89 | Dark brown | 190-192 | 62      | 0.48 |

Reagents and condition: (i) KOH, EtOH, reflux 3h; (ii) POCl₃, reflux 3h; H₂O, reflux 4 h; KOH; (iii) CICH₂COCl, TEA, DMF, reflux 2 h; (iv) K₂CO₃, DMF, reflux 10 h
3.2. Biological evaluation

The antibacterial operation in vitro was carried out against Gram-positive bacteria, including S. aureus, B. subtilis, and Gram-negative bacteria, including A. baumannii. P. aeruginosa. Many of the synthesized compounds 4(a-j) have been tested for antibacterial activity by calculating the inhibition zone in mm using the cup-plate agar diffusion method[22]. (Amoxicillin and Ciprofloxacin) have been used as a typical antibacterial activity medication. The observations are illustrated in Table 2.

If we display the (inhibition zone) data of some synthesized compounds 4(a-j) in Table (2), some significant findings are observed:

The first showed good activity against (P. aeruginosa) compounds (4d) (4 g), while only compounds (4d) (4 g) showed good activity against (B. subtilis). We also showed that some of the compounds (4b) (4h) have strong activity against (S. aureus), while no antibacterial activity against (A. baumannii) was seen in all compounds 4(a-j).

Table 1. The antibacterial efficacy of compounds synthesized

| Comp. No. | Concentration (mg / ml) | Zone of inhibition (in mm) | Gram-positive | Gram-negative |
|-----------|-------------------------|---------------------------|---------------|---------------|
|           |                         |                           | B. subtilis   | S. aureus     | A. baumannii  | P. aeruginosa |
| 4a        | 100                     | -                         | 10            | -             | 12            |
|           | 50                      | -                         | 7             | -             | 8             |
| 4b        | 100                     | -                         | 15            | -             | 12            |
|           | 50                      | -                         | 8             | -             | 9             |
| 4c        | 100                     | 11                        | -             | 13            |
|           | 50                      | 10                        | -             | 12            |
| 4d        | 100                     | 28                        | -             | 20            |
|           | 50                      | 17                        | -             | 15            |
| 4e        | 100                     | -                         | -             | 13            |
|           | 50                      | -                         | -             | 15            |
4. Conclusion

Benzimidazole compounds of thiadiazole moiety have been formed and structurally characterized using spectroscopic techniques. Pharmacological research has been conducted to examine the replacement effects on antibacterial function, with some variants exhibiting high to moderate activity against bacteria.

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