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Scientific paper

Synthesis, Characterization and Biological Activity Evaluation of Novel Quinoline Derivatives as Antibacterial Drug

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Abstract

Quinoline and its derivatives are a family with unique medicinal properties, including antibacterial effects. It was assumed that the four quinoline derivatives **1**, **2**, **3** and **4** had significant activity against pathogenic bacteria. These compounds were synthesized and characterized by TLC, IR, ^{1}H NMR, and ^{13}C NMR analyses. The biological activity of compounds was determined as inhibition zone (IZ) in mm. For compound **1** IZ was 19 ± 0.22 against *Klebsiella pneumoniae*, IZ was 18 ± 0.22 against *Bacillus subtilis*, and IZ was 17 ± 0.22 against *Staphylococcus aureus*. **2** displayed IZ of 18 ± 0.22 against both *Klebsiella pneumoniae* and *Bacillus subtilis*. **3** showed IZ of 17 ± 0.22 against *Staphylococcus aureus*. **4** displayed IZ of 21 ± 0.22, thus showing a higher inhibitory activity against *Escherichia coli*, than ciprofloxacin. These results demonstrate the potential of the synthesized compounds to work as antibacterial drugs against these strains by inhibiting or deactivating the target proteins.

Keywords: Quinoline derivatives; drug-resistant; pathogenic bacteria; *Klebsiella pneumoniae*; *Escherichia coli.*

1. Introduction

Bacteria are single-celled micro-organisms that exhibit great morphological diversity with dimensions ranging from 0.5–5 µm. There are only a few types of bacteria that cause disease. These types are called pathogens. Bacteria that inhabit the body naturally and peacefully can sometimes cause disease by producing harmful substances, invading tissues, or both. Among the most important bacterial diseases that may affect some individuals are cholera, diphtheria, dysentery, plague, pneumonia and tuberculosis. The most common and deadly bacterial diseases are respiratory infections and tuberculosis infection, which alone kill two million people each year.[1] Antibacterial drugs are antimicrobial compounds covering a range of effective medications that fight bacterial infections by killing or stopping them from reproducing.

The resistance to antibacterial drugs develops in some types of bacteria due to the acquisition of genes from other bacteria that have become resistant to antibacterial drugs or by mutations in the genes. Genes that enable bacteria to resist antibacterial drugs can be passed on to subsequent generations of the same bacteria, or sometimes to other types.[2] The more an antibacterial drug is used, the greater is the risk of developing resistance to it. For this reason, doctors try not to use antibiotics, unless necessary. Antibiotic-resistant bacteria can also be passed from person to person, becoming widespread globally in a relatively short period. They can also be transmitted from humans to animals, including those on farms.[3]

Among the various medicines, herbs,[4] nanoantibiotics,[5] and heterocyclic organic compounds, quinoline is an important building block in the construction of new medicinal drugs. It is nontoxic to humans by oral absorption and inhalation.[6] Quinolones are one of the most significant groups of antibacterial agents discovered in the last 50 years.[7] The development of quinolones dates back to the 1960s, when George Lesher discovered nalidixic acid by accident during the production of the antimalarial compound chloroquine. Then FDA (Food and Drug Administration) approved this compound for the urinary tract infections and against Gram-negative bacteria.[8] By adding fluorine, the fluoroquinolone family appeared, then FDA documented more than twenty compounds of this family

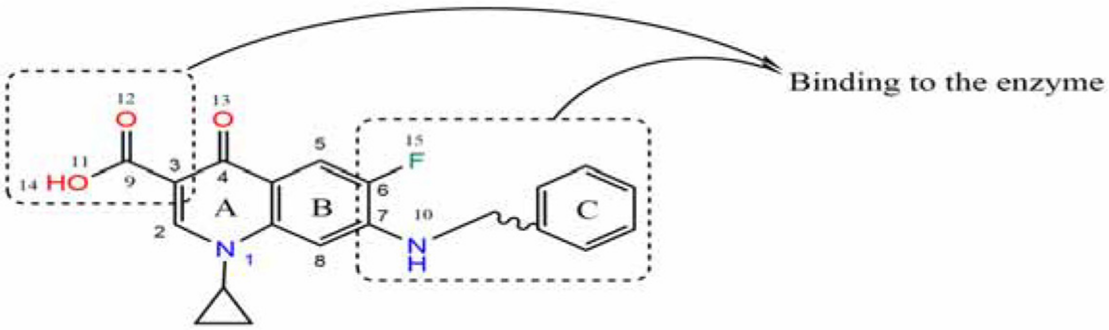
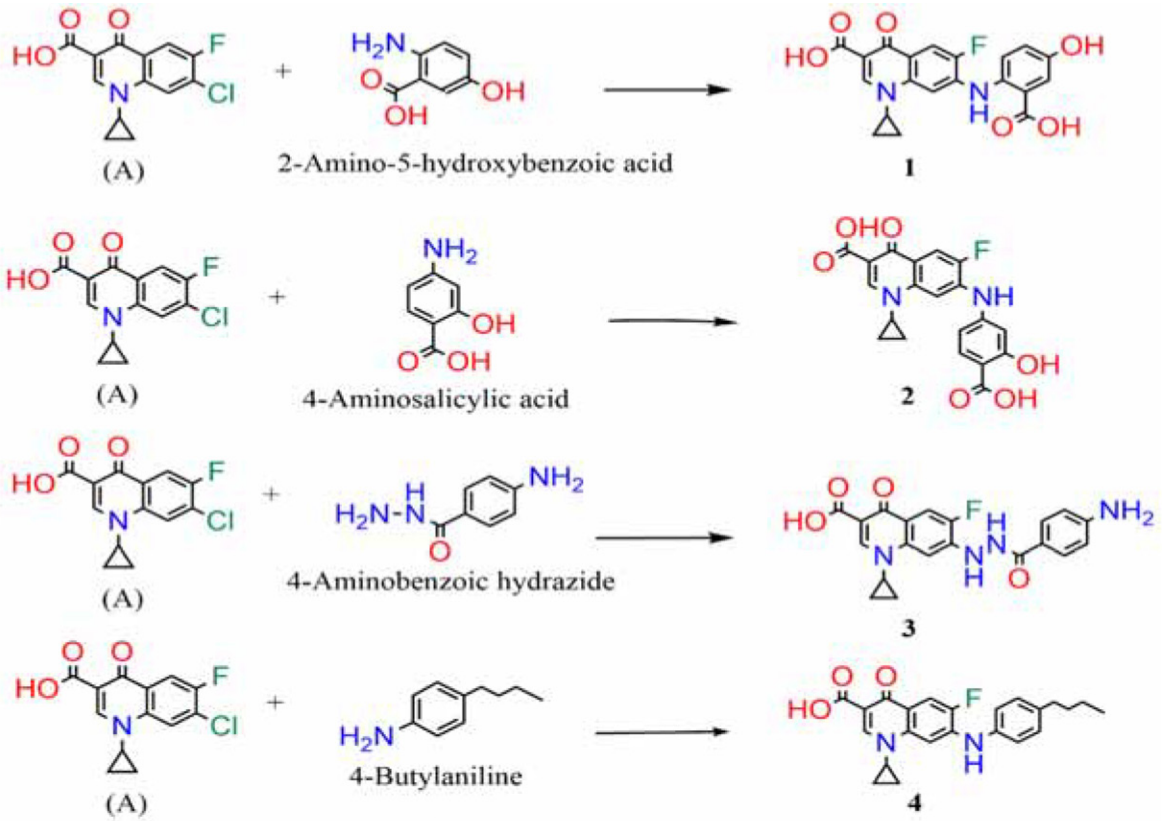


Figure 1. Enzymatic activity center in the fluoroquinolones.

circulating in the market with antimicrobial effects 1000 times stronger than nalidixic acid.[9] Fluorine's key features, at the position 6 (Figure 1), can influence pharmacological, pharmacodynamic and pharmacokinetic effects, as well as biological activity. Due to its electronic, lipophilic, and steric properties, including its strong electronegativity, low polarizability, solubility, hydrogen-bonding, tiny size, and steric effects, the fluorine atom is a significant constituent generally in drug design, particularly in quinolones.[10]

The incorporation of nitrogen into the ring at the position 7, fluoroquinolones have potent activity against Gram-positive respiratory pathogens. The use of a small additional groups at the position 8, such as methoxy and halide, increases the water solubility and anaerobic activity; in some cases it is even possible to switch from intravenous to oral application. When phototoxicity is considered, the methoxy group is preferred over the halide to avoid side effects as well as it is possible that its effectiveness lasts longer, thus reducing the effects of mutations.[11] Finally, the significant effect of the cyclopropyl group cannot be neglected for improve activity of the compounds.[12]

Because of the side effect of antibiotic drugs like quinoline compounds, there is a need for continuous design and development towards the goal of reducing these side effects (emerging of antibacterial resistance) hence the synthesis of novel quinoline derivatives is becoming increasingly essential.



Scheme 1. The synthesis of compounds **1**–**4**.

In this study, four quinoline derivatives: **1**, **2**, **3** and **4** were synthesized, being part of our theoretical study in the research (Kassar and Ezzat, 2023).[13] Characterization of the synthesized compounds was carried out by using melting point determination, pH, TLC, IR, ^{1}H NMR and ^{13}C NMR spectroscopy and then the study of the biological activity was performed.

2. Materials and Methods

All of the chemicals used in this research were of the maximum purity obtainable, and they were used directly from the producers without any further processing.

2. 1. Synthesis

281.67 mg (1 mmol) of 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (**A**) were weighed with a sensitive balance, then placed in a round-bottom flask with 10 mL of methanol. To synthesize **1**, 153.14 mg (1 mmol) of 2-amino-5-hydroxybenzoic acid were weight and added to **A**. The solution was heated under reflux while stirring for 2 h. Compound **2** was synthesized by weighting and adding 151.17 mg (1 mmol) of 4-aminobenzoic hydrazide to **A** to yield **2**, followed by the same steps as for the synthesis of **1**. Compound **3** was obtained by adding 153.14 mg (1 mmol) of 4-aminosalicylic acid to **A** followed by the same steps as for the synthesis of **1**. To yield product **4**, 0.17 mL of 4-butylaniline was used, followed by the same steps as for the synthesis of **1** (Scheme 1). After the reaction was finished, the product was placed in a blast drying oven FCD-3000 at 50 °C with a fan for 1 h to allow the methanol to evaporate and the product to dry. The experiment was repeated with dimethyl sulfoxide (DMSO) as the solvent, and the products were allowed to precipitate for 15 days.[14]

2. 2. Characterization

Thin-layer chromatography (TLC). Several solvent systems were tested for TLC on Echo silica gel F254 plates to monitor the reaction. The most suitable were tetrahydrofuran : cyclohexane 7 : 3 (solvent system I), and acetone : cyclohexane 5 : 5 (solvent system II). The spots were detected by using a UV lamp. Retention factors (R_f) and relative lipophilicities (R_m) being log [1 – R_f/R_f]) were determined.

Melting point measurements. The melting points of the products was determined by Electro-thermal Stuart melting point apparatus of finely powdered samples in open capillary tubes with one side closed with a heat source.

Infrared spectroscopy (IR). 2 mg of the products were dried in a blast drying oven at 50 °C. Then, from each compounds, an IR disc was prepared individually with 200 mg of dried KBr. Subsequently, the IR spectrum was recorded within the range of 400 cm^{-1} to 4000 cm^{-1} in the Department of Chemistry's research lab at the University of Anbar's College of Education for Women.

Nuclear Magnetic Resonance (NMR) Spectroscopy. ^{1}H and ^{13}C NMR spectra for the prepared compounds were recorded in DMSO-d_6 using a Bruker 400 MHz and a Jeol Lambda 500 MHz instrument at the research laboratory of the Department of Chemistry at the College of Education for Pure Sciences – University of Basra. Chemical shifts are given in ppm (δ). Multiplet, singlet, doublet, triplet, and quartet are denoted by the letters m, s, d, t, and q, respectively.

2. 3. Biological Activity

Two kinds of bacteria were used, Gram-negative bacteria *Escherichia coli* and *Klebsiella pneumoniae*. As Gram-positive bacteria, *Staphylococcus aureus* and *Bacillus subtilis* were used. These bacteria were diagnosed and cultured on eosin methylene blue (EMB) and nutrient agar medium for use in this experiment, and in measuring the deactivating capacity of the synthesized quinoline derivatives.

The deactivating capacity of the isolated bacteria of the compounds prepared, was tested by using the holes method. In this method the holes were saturated with (10 μL) of $1 \cdot 10^{-4}$ M of the compounds **1**, **2**, **3**, **4** and ciprofloxacin, then left for about 15 min in order to spread on the medium. Sequentially, incubated at 25 °C for 24 h. The deactivation diameters were measured by a special ruler designed for this purpose.

3. Results

3. 1. General Characteristics

Compound 1. $C_{20}H_{15}FN_2O_6$: greyish brown powdery product, yield 3.226 g (81%); $R_f = 0.85$, $R_m = -0.75$ (solvent system I). $R_f = 0.61$, $R_m = -0.194$ (solvent system II). m.p. 228–230 °C. FTIR: ν 2500–3080, 1726, 1610, 1586, 1497, 1250–1400, 3227 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.61 (s, 1H), 8.74 (s, 1H), 8.65–8.60 (m, 2H), 8.50 (d, J = 6.1 Hz, 1H), 8.30 (s, 1H), 8.25 (s, 2H), 8.18 (d, J = 9.0 Hz, 1H), 8.06 (s, 1H), 7.09 (d, J = 2.9 Hz, 2H), 6.77 (dd, J = 8.7, 2.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 3.84 (q, J = 5.4 Hz, 1H), 1.32 (t, J = 6.6 Hz, 2H), 1.21 (d, J = 4.2 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 177.18, 177.15, 169.86, 165.82, 156.82, 154.34, 149.73, 147.02, 145.25, 138.65, 127.67, 127.47, 125.92, 125.85, 123.49, 121.69, 118.13, 115.65, 112.44, 112.21, 110.38, 107.94, 40.54, 40.33, 40.12, 39.91, 39.71, 39.50, 39.29, 36.78, 8.14.

Compound 2. $C_{20}H_{15}FN_2O_6$: yellowish brown powdery product, yield 3.345 g (84%); $R_f = 0.97$, $R_m = -1.50$ (solvent system I). $R_f = 0.45$, $R_m = -0.087$ (solvent system II). m.p. 193–196 °C. FTIR: ν 3094, 3385, 1726, 3499, 1610 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 14.62 (s, 1H), 11.38 (s, 1H), 8.75 (s, 1H), 8.52 (d, *J* = 6.1 Hz, 1H), 8.19 (d, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 6.11–5.89 (m, 3H), 3.86 (tt, *J* = 7.6, 4.0 Hz, 1H), 1.33 (t, *J* = 6.5 Hz, 2H), 1.21 (p, *J* = 5.1 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm): 177.18, 177.16, 172.56, 165.81, 163.88, 158.51, 156.82, 156.27, 154.34, 150.19, 149.75, 138.67, 131.90, 129.87, 127.67, 127.48, 125.93, 125.86, 121.72, 112.44, 112.22, 107.94, 106.67, 105.89, 103.77, 101.43, 100.54, 98.94, 40.56, 40.35, 40.15, 39.94, 39.73, 39.52, 39.31, 36.80, 8.15.

Compound 3. $C_{20}H_{17}FN_4O_4$: off white powdery product, yield 3.130 g (79%); R_f = 0.81, R_m = –0.62 (solvent system I). R_f = 0.61, R_m = –0.194 (solvent system II). m.p. 208–211 °C. FTIR: ν 3434, 3355, 3306, 3227, 2600–3031, 1734, 1610 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.28 (s, 2H), 8.75 (s, 1H), 8.51 (d, *J* = 6.1 Hz, 1H), 8.19 (d, *J* = 9.0 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 4H), 6.52 (d, *J* = 8.4 Hz, 4H), 5.59 (s, 3H), 3.89–3.82 (m, 1H), 1.33 (d, *J* = 6.7 Hz, 2H), 1.21 (q, *J* = 4.0, 3.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 177.19, 177.16, 166.92, 165.83, 156.83, 154.35, 151.99, 149.75, 138.68, 128.88, 127.68, 127.48, 125.94, 125.87, 121.71, 120.37, 113.06, 112.45, 112.22, 107.96, 40.57, 40.36, 40.15, 39.94, 39.74, 39.53, 39.32, 36.79, 8.15.

Compound 4. $C_{23}H_{23}FN_2O_3$. light brown powdery product, yield 2.997 g (76%); R_f = 0.93, R_m = –1.12 (solvent system I). R_f = 0.74, R_m = –0.454 (solvent system II). m.p. 235–238 °C. FTIR: ν broad and very strong band 2800–3500, 2967, 2858, 1614, 1561, 1395, 1313, 1211. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.81 (s, 1H), 8.57 (d, *J* = 6.1 Hz, 1H), 8.25 (d, *J* = 8.9 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.53 (d, *J* = 8.1 Hz, 1H), 3.92 (dt, *J* = 7.2, 3.3 Hz, 1H), 2.57 (d, *J* = 1.7 Hz, 2H), 2.43 (t, *J* = 7.6 Hz, 1H), 1.50 (p, *J* = 7.4 Hz, 1H), 1.44–1.22 (m, 6H), 0.92 (*t*, *J* = 7.3 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 177.19, 177.16, 165.86, 156.83, 154.35, 149.76, 146.69, 138.68, 138.66, 129.79, 129.03, 127.69, 127.49, 125.93, 125.86, 121.72, 114.45, 112.44, 112.21, 107.96, 40.52, 40.31, 40.10, 39.89, 39.68, 39.47, 39.26, 36.79, 34.50, 34.10, 22.14, 14.29, 8.14.

4. Discussion

4. 1. Characterization of Compound 4

The synthesis of the selected fluroquinolones was demonstrated by IR analysis, which revealed significant absorption bands. Firstly, a broad and very strong band between 2800–3500 cm^{-1} belongs to the carboxylic group. Medium 2967 cm^{-1} to the stretching vibration of the methyl group, while small 2858 cm^{-1} to the stretching of ethylene group. Medium band at 1614 cm^{-1} corresponds to the α,β-unsaturated ketone, 1561 cm^{-1} is N–H bending, 1395 cm^{-1} O–H bending of carboxylic acid, 1313 cm^{-1} is C–F stretching, medium 1211 cm^{-1} C–N stretching (Figure S1).

The synthesized compounds were characterized using **^{1}**H NMR and **^{13}**C NMR spectroscopy, Characteristic signals for compound **4** in its ^{1}H NMR spectrum are: δ 0.93 to HC29 (t, 2H; H_2C28), 1.25 to H_2C17 (q, 3H; H_2C16, HC15), 1.32 to H_2C28 (m, 5H: H_3C29, H_2C27), 6.53 to HC22,24 (d, 1H; HC21,HC25), 8.24 to HC6 (d, 1F; FC1) 8.8 to HC8 (s). Signals between δ 3.3–3.5 corresponds to water and may indicate sample wetting, as it is known that DMSO is very hygroscopic, while a signal at δ 2.5 is non-deuterated DMSO. In this case, the NH signal either disappears completely or may appear as a broad signal extremely close to the solvent signals (Figure S2).

Characteristic signals for compound **4** in its ^{13}C NMR spectrum are: δ 177.19 and 165.86 to carbonyl C10 and C12, (d, 156.83) to C1, 36.79 to C26, 34.10 to C27, 22.14 to C28, 14.29 to C29, 8.14 to C16 and C17 (Figure S3).

4. 2. Characterization of Compound 1

The absorption bands in IR spectrum of **1** are depicted in Figure S4: the broadened bands at lower frequencies from 2500 to about 3080 cm^{-1} are for the stretching vibration of carboxylic hydroxyl, the C=O bond is weakened by intermolecular hydrogen bonding, lowering the stretching frequency to 1726 cm^{-1}. The band at 1610 cm^{-1} belongs to the cyclic carbonyl, at 1586 cm^{-1} is due to the stretching vibration of the aromatic C=C, and at 1497 cm^{-1} is due to the C–O. The variation in the electronic environment; causes the bond's absorption of C–N shift depending on its location, leading the band to expand from 1250 cm^{-1} to 1400 cm^{-1}. Finally, the characteristic 3227 cm^{-1} band is caused by the stretching vibration of *para*-hydroxyl, with the disappearance of the secondary N–H, often included within the domain of the carboxyl group.

Characteristic signals for compound **1** in its ^{1}H NMR spectrum are: δ 3.88 to HC15 (m, 4H; H_2C16, H_2C17), 7.1 to HC24 (s), 8.19 to HC6 (d, 1F; FC1), 8.50 to HC3 (d, 1H; NH), 8.63 to HO26 (s), 14.6 to HO28 carboxylic proton (Figure S5).

Characteristic signals for compound **1** in its ^{13}C NMR spectrum are: 177.18 to C10, 169.86 to C27, 165.82 to C12, 156.82 to C23, (d,154.34) to C1, 149.73 to C8, 147.02 to C20 (Figure S6).

4. 3. Characterization of Compound 2

Despite having the same functional groups as **1**, IR spectrum of compound **2** revealed considerable variances due to the varied site-substitution on the benzene ring. The intensity of the carboxylic hydroxyl band was reduced by the presence of the hydroxyl close to the carboxyl. The degree of H-bonding determines the position and shape of this band.

The original O–H bond is lengthened during hydrogen bonding. As a result, the bond is weakened, the bond force constant is reduced, as well as the stretching frequency. The *ortho*-carboxylate hydroxyl is detected at 3094

Table 1. Inhibitory activity of the synthesized compounds and comparison with ciprofloxacin.

	Diameter of inhibition zone (in mm) ±0.22 mm			
Compound	***E. coli***	***S. aureus***	***B. subtilis***	***K. pneumoniae***
1	17	17	18	19
2	14	13	18	18
3	16	17	16	13
4	21	13	15	14
Ciprofloxacin	19	16	19	17

cm^{-1}, the secondary N–H (single band) is recorded at 3385 cm^{-1}, the carbonyl is noted at 1726 cm^{-1}, and the overton band for the same group is noted at 3499 cm^{-1}, while 1610 cm^{-1} corresponds to the cyclic carbonyl (Figure S7).

Characteristic signals for compound **2** in its ^{1}H NMR spectrum are: δ 1.20 to H_2C17 (q, 3H; H_2C16, HC15. 6.77 to HO29, 8.51 to HC6 (d, 1F; FC1), 11.38 to HO13 (s) and 14.62 to HO27 of carboxyl (s), 3.40 and 2.51 to water and DMSO, respecitvely (Figure S8).

Characteristic signals for compound **2** in its ^{13}C NMR spectrum are: 177.18, 172.56 and 165.81 to C10, C26 and C12 of carbonyl respectively, (d, 158.51) to C1, 36.80 to C15, 8.15 to C16 and C17 (Figure S9).

4. 4. Characterization of Compound 3

IR spectrum of compound **3** (Figure S10) shows the band at 3434 cm^{-1} belonging to the N–H adjacent to the carbonyl, where the electronic withdrawal of the carbonyl increases the bond strength constant, pushing the band towards a higher frequency. The primary amine on the benzene ring at the *para*-site (dual band) is represented by the 3355 cm^{-1} and 3306 cm^{-1} bands. The 3227 cm^{-1} is for N–H bound to the quinolone ring. The broad band extending from 2600–3031 cm^{-1} is for the quinolone's terminal carboxylate, 1734 cm^{-1} is due to the quinolone ring ketone, 1610 cm^{-1} to the aniline ring-linked ketone.

Characteristic signals for compound **3** in its ^{1}H NMR spectrum are: δ 1.20 to H_2C17 (q, 3H; H_2C16, HC15), 5.59 to HN29 (s), 6.53 to HC25 and HC27 (d, 1H; HC24, HC28), 9.28 to HN20 (s), 3.40 and 2.51 correspond to H_2O and DMSO which cause H-N19 disappearance (Figure S11).

Characteristic signals for compound **3** in its ^{13}C NMR spectrum are: 177.19 to C10, 166.92 to C12, 165.83 to C21, 156.83 to C26, (d,154.35) to C1 (Figure S12).

5. Biological Activity

The antibacterial activity of the synthesized compounds was studied on four previously diagnosed isolates of Gram-positive (*S. aureus* and *B. subtilis*) and Gram-negative (*E. coli* and *K. pneumoniae*) bacteria. Experimental results for the compound **1** showed the following inhibition zones (IZ): 19 ± 0.22 mm against *K. pneumoniae*, 18 ± 0.22 mm against *B. subtilis*, and 17 ± 0.22 mm against *S. aureus*. Compared with ciprofloxacin, the inhibitory activity of the compound **1** was higher against *K. pneumoniae* and *S. aureus*, but lesser against *B. subtilis* as shown in Table 1. In designing drugs with fewer side effects, this means that the compound's influence on non-pathogenic bacteria is lessened, which is an important consideration.

For compound **2**, experimentally, the effect was equal by IZ 18 ± 0.22 mm. Compared with ciprofloxacin, the inhibitory activity of **2** was higher against *K. pneumoniae*, and lesser against *B. subtilis* as shown in Table 1. Compound **3** showed a higher inhibitory activity against *S. aureus* (IZ 17 ± 0.22 mm), than ciprofloxacin (Table 1). Compound **4** showed a higher inhibitory activity against *E. coli* (IZ 21 ± 0.22 mm), than that of ciprofloxacin (Table 1).

These results demonstrate the potential of the synthesized compounds as antibacterial drugs against these strains by inhibiting or activating the target proteins.

6. Conclusions

Four novel quinoline derivatives **1**, **2**, **3** and **4** were successfully synthesized and characterized by TLC, IR, ^{1}H and ^{13}C NMR spectroscopy confirming the success of the synthetic procedures. In comparison to ciprofloxacin, *in vitro* evalution of the synthesized compounds showed that two of them demonstrated good antibacterial activity, suggesting the potential for their future use as an alternative treatment after undertaking the necessary research.

Supporting Information

Scans of IR, ^{1}H and ^{13}C NMR spectra of compounds **1–4**.

7. References

1. F. Godoy-Vitorino, *Ann. Transl. Med.* **2019**, *7(14),* 342–342. **DOI:**10.21037/ATM.2019.06.56
2. C. L. Ventola, *Pharm. Ther.* **2015**, *40(4)*, 277. **DOI:**Article.

3. X.-F.Shang, S. L. Morris-Natschke, Y.-Q. Liu, X. Guo, X.-S. Xu, M. Goto, J.-C. Li, G.-Z. Yang, K.-H. Lee, *Med. Res. Rev.* **2018**, *38(3)*, 775. **DOI:**10.1002/MED.21466.
4. A. Alabdali, M. Kzar, S. Chinnappan, R. Mogana, S. I. Khalivulla, H. Rahman, B. M. Abd Razik, *Res. J. Pharm. Technol.* **2021**, *14(12)*, 6741–6746. **DOI:**10.52711/0974-360X.2021.01164.
5. A. Y. M. Alabdali, M. S. Kzar, S. Chinnappan, R. R. Mani, M. Selvaraja, K. J. Wen, L. Sally, F. W. Kuang, *Int. J. App. Pharm.* **2022**, pp 34–39. **DOI:**10.22159/ijap.2022v14i3.43508.
6. M. De Souza, *Mini-Rev. Med. Chem.* **2005**, *5(11)*, 1009–1017. **DOI:**10.2174/138955705774575246.
7. M. G. Ferlin, G. Chiarelotto, F. Antonucci, L. Caparrotta, G. Froldi, *Eur. J. Med. Chem.* **2002**, *37(5)*, 427–434. **DOI:**10.1016/S0223-5234(02)01355-7.
8. T. D. M. Pham, Z. M. Ziora, M. A. T. Blaskovich, *MedChemComm* **2019**, *10*, 1719–1739. **DOI:**10.1039/C9MD00120D.
9. V. T. Andriole. *Clin. Infect. Dis.* **2005**, *41(2)*, S113–S119. https://www.jstor.org/stable/4463376.
10. K. J. Aldred, R. J. Kerns, N. Osheroff, *Biochemistry* **2014**, *53*, 1565–1574. **DOI:**10.1021/BI5000564.
11. J. J. Champoux, *Ann. Rev. Biochem.* **2003**, *70*, 369–413. **DOI:**10.1146/ANNUREV.BIOCHEM.70.1.369.
12. R. Musiol, J. Jampilek, V. Buchta, L. Silva, H. Niedbala, B. Podeszwa, A. Palka, K. Majerz-Maniecka, B. Oleksyn, J. Polanski, *Bioorg. Med. Chem.* **2006**, *14(10)*, 3592–3598. **DOI:**10.1016/j.bmc.2006.01.016
13. M. J. Kassar, M. O. Ezzat, *Egypt. J. Chem.* **2023**, *66(5)*, 119–128. **DOI:**10.21608/EJCHEM.2022.151949.6577.
14. Y. Mirzaie, J. Lari, H. Vahedi, M. Hakimi, *Russ. J. Gen. Chem.* **2016**, *86(12)*, 2865–2869. **DOI:**10.1134/S1070363216120525.

Povzetek

Kinolin in njegovi derivati so družina spojin s posebnimi medicinskimi lastnostmi, vključno s protibakterijskimi učinki. Predvideli smo, da bodo štirje kinolinski derivati (spojine **1**, **2**, **3** in **4**) imeli opazen učinek na patogene bakterije. Spojine smo sintetizirali in jih karakterizirali s TLC, IR, ^{1}H NMR in ^{13}C NMR spektroskopijo. Biološko aktivnost spojin smo določili kot območje inhibicije (IZ) v mm. Za spojino **1** je IZ proti *Klebsiella pneumoniae* znašal 19 ± 0.22, proti *Bacillus subtilis* je bil 18 ± 0.22, proti *Staphylococcus aureus* pa 17 ± 0.22. Spojina **2** je proti *Klebsiella pneumoniae* in proti *Bacillus subtilis* izkazala IZ 18 ± 0.22. Za spojino **3** je IZ proti *Staphylococcus aureus* znašal 17 ± 0.22. Spojina **4** je proti *Echerichia coli* izkazala IZ vrednost 21 ± 0.22, kar predstavlja večjo inhibitorno aktivnost kot ciprofloksacin. Rezultati kažejo, da so sintetizirane spojine potencialno uporabne proti tem vrstam bakterij, saj inhibirajo ali deaktivirajo izbrane proteine.