

Modification on Ciprofloxacin Moiety to Synthesize Some New Derivatives with Screening Antibacterial Activity

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Abstract

A major global public health problem is the emergence of antimicrobial resistance to common commercial medications. Therefore, there is an urgent need for new antimicrobials with enhanced biological activity. In this regard, in this study 5 novel Quinolone derivative A, B, C, D, and E were synthesized and their structure was analyzed using UV light, FTIR, ¹H NMR, and ¹³C NMR techniques. The structure of synthesized compounds was investigated. The well diffusion assay method was used to test the synthetic compounds' antibacterial properties in vitro against two Gram-positive (*Staphylococcus aureus* and *Streptococcus pyogenes*) and two Gram-negative (*Escherichia coli* and *Klebsiella pneumoniae*) bacteria. Ciprofloxacin drug was used as an antibiotic standard. Best activity was shown by compound C against *E. coli* with an inhibition zone of 30mm and 33 mm at 250 and 500 µg/mL respectively. While compound B in *Staphylococcus aureus* has high inhibition zone of 42mm and 47mm at 250 and 500µg/mL respectively. However compound D in *Klebsiella pneumoniae* has high inhibition zone of 32mm and 35mm at 250 and 500µg/mL respectively, while compound A for *Streptococcus pyogenes* has inhibition zone of 45mm and 47mm at 250 and 500µg/mL respectively.

Keywords: Anti-bacterial, Cell line, Ciprofloxacin, Quinolone, Well diffusion assay.

Introduction

Bacterial infections represent a prevalent etiology of chronic diseases, exhibiting increased morbidity and mortality rates, and affecting a vast population.¹ Various bacterial strains have infected one-third of the world's population². Despite advancements in Recently, Quinolone heterocyclic chemistry has garnered considerable attention due to its potential biological and pharmacological effects. For organic and pharmaceutical chemists, this system has proven to be an excellent scaffold. Quinolone derivatives, on the other hand, have been widely explored as bioactive chemicals⁴ Quinolone and its derivatives have considerable applications in

the 21st century, bacteria persist as a formidable peril to human health, demanding immediate research efforts to discover compounds that exhibit superior antibacterial properties and broad-spectrum activities.³

medicines and organic chemistry. They exhibit anti malarial^{5,6}, anticancer^{7,8}, antibacterial^{9,10}, antifungal^{11,12}, therapeutic anti diabetic¹³, antiviral¹⁴, antioxidant¹⁵, anti-inflammatory¹⁶, anti proliferative¹⁷, and anti-tubercular¹⁸.

Quinolone has the chemical formula C₉H₇N and is a rare hetero-aromatic molecule in which 10 electrons

flow throughout the structure. Quinolone is a bicyclic heterocyclic system that consists of pyridine and a six-membered benzene ring¹⁹

Bacteria are single-celled microorganisms with sizes ranging from 0.5 to 5 μm and a wide variety of morphologies. Numerous species of bacteria inhabit the skin, respiratory passages, mouths, gastrointestinal tracts, reproductive systems, and other body parts of both humans and animals^{20, 21}.

Approximately 30% of individuals have *Staphylococcus aureus*, a gram-positive bacterium, in their nasal passages, which is associated with various clinical disorders. Another significant gram-positive bacterial pathogen, *Streptococcus pyogenes*, is responsible for acute bacterial infections in the human oropharynx and serves as the causative agent of scarlet fever^{22, 23}.

The *Klebsiella pneumoniae*, is Gram-negative characterized as rod-shaped, lactose-fermenting, non-motile bacteria with an encapsulated structure, has emerged as a notable pathogen causing nosocomial infections^{24, 25}. On other hand *Escherichia coli* is a rod-shaped, gram-negative bacteria that is typically found in the lower intestine of endothermic (warm-blooded) species²⁶.

This was the result of later modifications and attempts to increase the antibacterial efficacy by adding chemical additives. One of the most drastic

of these changes was the addition of fluorine to the molecule in 1996. Norfloxacin is the first member of the fluoroquinolone (FQ) family approved for human use. This family was created by adding fluorine. A year later, ciprofloxacin with an N-1 cyclopropyl group was introduced. Then the US Food and Drug Administration discovered more than 20 chemicals of this class that were commercially available with antibacterial properties that were 1,000 times stronger than nalidixic acid. Therefore, the prepared derivatives are modified ciprofloxacin derivatives. Therefore, fluoroquinolone is a bacterial antibiotic that belongs to the fluoroquinolone family. It is effective against most gram-negative and gram-positive bacteria, so it is used to treat different types of bacterial infection²⁷.

In this work, we have synthesized new heterocyclic Quinolone derivatives and analyzed them by using common spectroscopic techniques including nuclear magnetic resonance spectroscopy and the infrared, their structures have been completely described. The antibacterial activity of each produced molecule has been assessed "in vitro" using against two Gram-positive *Staphylococcus aureus* (*s.aureus*) and *Streptococcus pyogenes* (*s.pyogenes*) and two Gram-negative *Escherichia coli* (*E.coli*) and *Klebsiella pneumoniae* (*K.pneumoniae*) bacteria.

Materials and Methods

General Method

All Chemical reagents and solvents were used as received and without any purification. Open capillary tubes were used to measure the melting points by using Electro-thermal Stuart melting point apparatus, which were then left uncorrected. On an aluminum plate, a layer of silica gel, GF254 (Merck) 0.2 mm thick, was used for analytical thin-layer chromatography (TLC). An UV lamp was used to find the spots. A Perkin-Elmer BX Spectrometer (400-4000 cm^{-1}) was used to record the Fourier-transform Infrared (FTIR) spectra of several substances as KBr pellets. Using a Bruker 400 MHz and a Jeol Lambda 500 MHz and dimethyl sulfoxide (D6) as a solvent, nuclear magnetic resonance (NMR) spectrum were recorded.

Chemistry

Five derivatives were synthesized, scheme 1 shows the synthesis derivatives and confirmed by using (FTIR), ¹H and ¹³C (NMR) spectroscopy. FTIR spectroscopy was used to characterize the specific functional groups present in the pure products. All of the chemicals used in this research were of the maximum purity obtainable and they were used directly from the producer without further processing. The progress of the reaction was monitored by thin layer chromatography (7:3 tetrahydrofuran, cyclohexane) have the best results in same eluent in all derivatives.

1. Synthesis of Derivative (A)

15 mL of methanol were put in round flask, (1g) 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and (0.5g) 3-Aminopyrazine-2-carboxylic acid were added. The

mixture was boiled under reflux using water condenser for five hours. The products were produced by the solvent evaporating under reduced pressure. The solid product was collected. It has the chemical formula: $C_{18}H_{13}FN_4O_5$. $R_f=0.83$ with solvent system(7:3) tetrahydrofuran, cyclohexane, white powder; m.p: 200-202 °C. IR :medium peak at 3467cm^{-1} which indicates the O-H carboxylic while medium sharp peak at the 3328cm^{-1} indicates that the N-H stretching and C-H aromatic are recorded at 3109cm^{-1} - 3026cm^{-1} ,the C-H aliphatic is noted at 2975cm^{-1} asymmetrical cm^{-1} stretch -2880cm^{-1} symmetrical stretch, the carbonyl carboxylic group C=O is recorder at 1718cm^{-1} while 1612cm^{-1} for the C=O carbonyl keton group, 1590cm^{-1} Return to the C=C, 1560 to the C=N, 1355cm^{-1} to the C-N and finally, 1259cm^{-1} appeared at C-F²⁸. ¹H NMR (400 MHz, DMSO) δ 8.77 – 8.70 (m, 1H), 8.48 (d, $J = 5.9$ Hz, 1H), 8.24 (s, 3H), 7.88 (s, 2H), 7.40 (s, 4H), 3.86 (s, 1H), 1.22 (s, 2H). ¹³C NMR (101 MHz, DMSO) δ 177.14, 168.34, 165.79, 156.55, 148.93 (d, $J = 157.4$ Hz), 138.63, 132.48, 127.56 (d, $J = 20.1$ Hz), 124.12, 121.67, 112.30 (d, $J = 22.9$ Hz), 107.95, 36.79, 8.15²⁹.

2. Synthesis of Derivative B

15 mL of methanol were placed in round flask, (1g) 7-Chloro-1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxoquinoline-3-carboxylic acid and (0.5g) 3-amino 4-Hydroxy benzoic acid were added. The mixture was boiled under reflux using water condenser for five hours. The products were produced by the solvent evaporating under reduced pressure. The solid product was collected. $R_f=0.96$ with solvent system (7:3) tetrahydrofuran, cyclohexane, orange powder; yield 90%; mp 230-232 °C, it has the chemical formula: $C_{20}H_{15}FN_2O_6$. IR: the band 3469cm^{-1} belongs to the O-H carboxylic group and overlaps with phenol. The N-H is noted at 3352cm^{-1} . The 3109cm^{-1} for C-H aromatic while C-H aliphatic asymmetrical and C-H symmetrical appeared at 2981cm^{-1} - 2925cm^{-1} respectively. At 1724cm^{-1} - 1704cm^{-1} for the carbonyl carboxylic and 1676cm^{-1} for the carbonyl keton. The band C=C appeared at the 1612cm^{-1} - 1465cm^{-1} . The C-F is noted at the 1305cm^{-1} and finally the C-O is recorded at 1257cm^{-1} ²⁸. ¹H NMR (400 MHz, DMSO) δ 9.82 (s, 2H), 8.78 – 8.71 (m, 1H), 8.55 – 8.46 (m, 1H), 8.23 – 8.14 (m, 1H), 7.25 – 7.18 (m, 2H), 7.12 – 7.03 (m, 2H), 6.73 – 6.63 (m, 2H), 3.86 (s, 1H), 1.33 (s, 2H), 1.21 (s, 1H). ¹³C NMR (101 MHz, DMSO) δ 177.16, 168.22, 165.80, 154.34,

149.24 (d, $J = 98.1$ Hz), 137.73 (d, $J = 183.6$ Hz), 127.57 (d, $J = 20.7$ Hz), 125.92, 122.20, 121.69, 119.45, 115.59, 113.97, 112.33 (d, $J = 22.7$ Hz), 107.96, 36.79, 8.15²⁹.

Synthesis of Derivative C

15 mL of methanol were put in round flask, (1g) 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and (0.5g) 2-amino benzohydrzide were added. The mixture was boiled under reflux using water condenser for five hours. The products were produced by the solvent evaporating under reduced pressure. $R_f = 0.82$ with solvent system (7:3) tetrahydrofuran, cyclohexane, crystal gold,: m.p= 108 - 110°C . The chemical formula is: $C_{20}H_{17}FN_4O_4$. IR : the bands appeared at 3442cm^{-1} for the stretching vibration of the carboxylic group with overlapping with N-H₂ where NH₂ is noted at ν 3442cm^{-1} - 3325cm^{-1} asymmetrical stretch and symmetrical stretch respectively, the C-H aromatic is recorder at the ν 3028cm^{-1} , the N-H is noted 3176cm^{-1} while C-H aliphatic appeared in 2935cm^{-1} - 2830cm^{-1} asymmetrical and symmetrical respectively and C=O carboxylic group appeared at 1730cm^{-1} . The range 1699cm^{-1} belongs to keton group, 1620cm^{-1} due to the amide group, and 1577cm^{-1} to C=C. and 1319cm^{-1} indicated the C-F. Finally, at 1261cm^{-1} back to C-O²⁸. ¹H NMR (400 MHz, DMSO) δ 9.28 (s, 1H), 8.75 (s, 1H), 8.51 (d, $J = 6.1$ Hz, 1H), 8.19 (d, $J = 9.0$ Hz, 1H), 7.62 (s, 0H), 7.53 (d, $J = 8.3$ Hz, 3H), 6.61 (s, 1H), 6.52 (d, $J = 8.4$ Hz, 3H), 5.59 (s, 3H), 3.86 (tt, $J = 7.5, 4.0$ Hz, 1H), 1.33 (d, $J = 6.7$ Hz, 1H), 1.21 (q, $J = 4.0, 3.4$ Hz, 1H). ¹³C NMR (101 MHz, DMSO) δ 177.18 (d, $J = 2.7$ Hz), 166.92, 165.83, 156.83, 155.59 – 148.04 (m), 138.68, 128.88, 127.58 (d, $J = 20.2$ Hz), 125.90 (d, $J = 6.9$ Hz), 121.71, 120.37, 113.06, 112.34 (d, $J = 22.8$ Hz), 107.96, 36.79, 8.15²⁹.

Synthesis of Derivative D

15 mL of methanol were placed in round flask, (1g) 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and (0.5g)2,6-di amino toluene were added. the mixture was boiled under reflux using water condenser for five hours. The products were produced by the solvent evaporating under reduced pressure. $R_f = 0.92$ with solvent system (7:3) tetrahydrofuran, cyclohexane. Crystal Black; m.p= 92 - 90°C . The chemical formula is: $C_{20}H_{18}FN_3O_3$. IR: the band 3446cm^{-1} which indicates to the carboxylic acid group. The NH₂

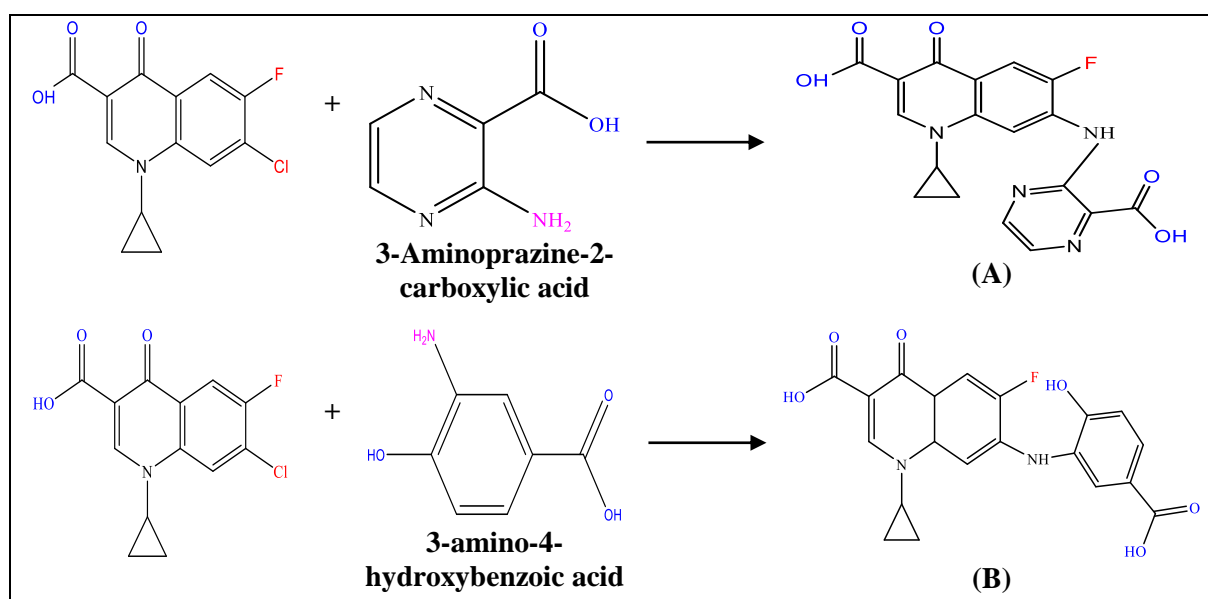
bond is noted at the rang 3423cm^{-1} - 3396cm^{-1} asymmetrical stretch and symmetrical stretch reticently . The band 3245cm^{-1} belongs to the N-H, 3105cm^{-1} due to the stretchy vibration of the aromatic C-H, and 3074cm^{-1} - 3051cm^{-1} cm^{-1} back to C-H aliphatic asymmetrical starch and symmetrical stretch reticently . the band 1730cm^{-1} back to carboxylic group while 1614cm^{-1} for the keton group. At the band 1560cm^{-1} - 1544cm^{-1} refers to the C=C while at the 1338cm^{-1} for the C-F and finally appeared at C-O at the 1259cm^{-1} ²⁸. ¹H NMR (400 MHz, DMSO) δ 14.62 (s, 2H), 8.75 (s, 2H), 8.52 (d, $J = 6.1$ Hz, 1H), 8.19 (d, $J = 9.0$ Hz, 1H), 7.41 (d, $J = 8.6$ Hz, 1H), 6.03 (dd, $J = 34.3, 7.1$ Hz, 3H), 5.96 (s, 1H), 3.86 (dt, $J = 7.2, 3.5$ Hz, 1H), 1.33 (t, $J = 6.5$ Hz, 3H), 1.21 (p, $J = 5.1$ Hz, 3H). ¹³C NMR (101 MHz, DMSO) δ 177.17 (d, $J = 2.7$ Hz), 172.56, 164.85 (d, $J = 194.7$ Hz), 160.22 – 152.63 (m), 149.75, 138.67, 130.88 (d, $J = 204.6$ Hz), 127.57 (d, $J = 20.0$ Hz), 125.89 (d, $J = 6.6$ Hz), 121.72, 112.33 (d, $J = 22.8$ Hz), 107.94, 106.67, 105.89, 103.77, 101.43, 100.54, 98.94, 36.80, 8.15 ²⁹.

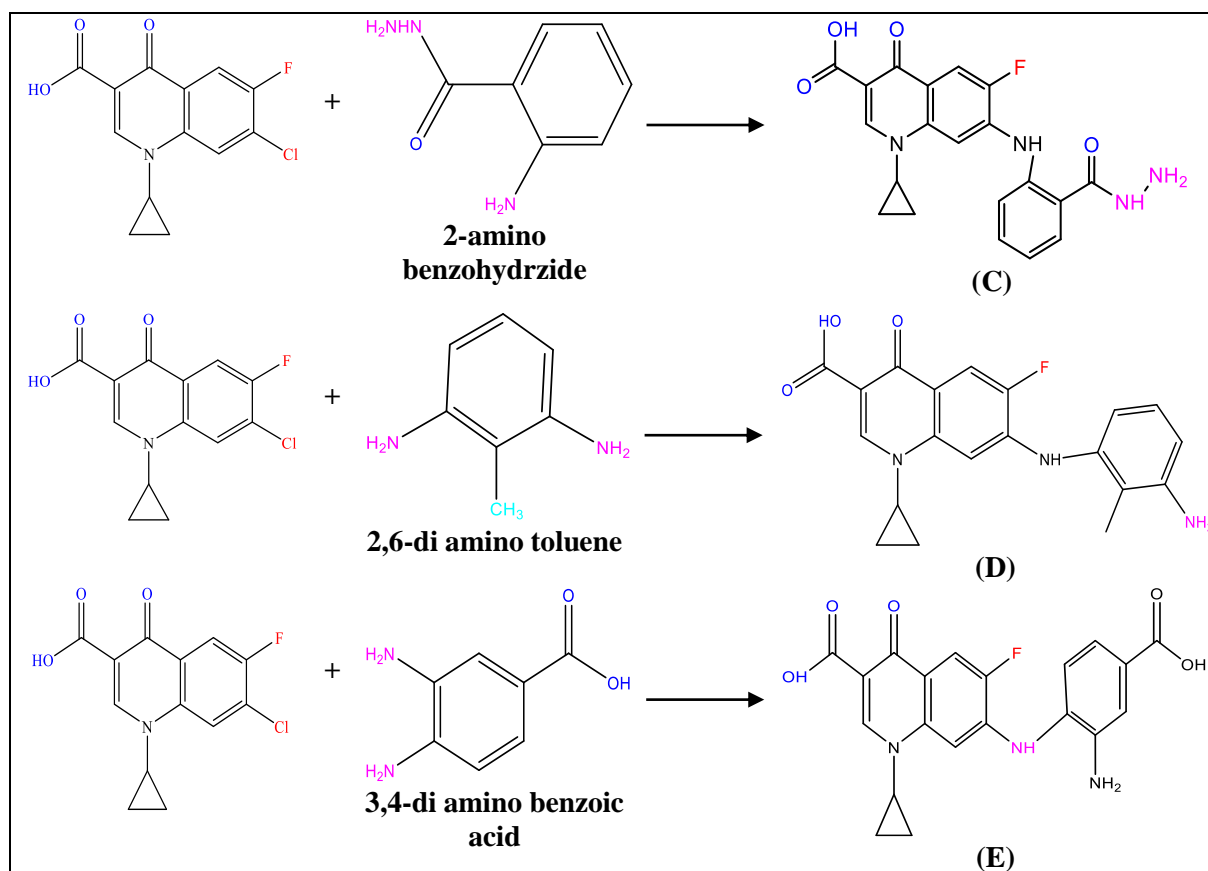
Synthesis of Derivative E

15 mL of methanol in round flask, (1g) 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and (0.5g)3,4-di amino benzoic acid were added. The mixture was boiled under reflux using water condenser for five hours. The products were produced by the solvent evaporating under reduced pressure. $R_f = 0.92$ with solvent

system (7:3) tetrahydrofuran, cyclohexane . Crystal gold; m.p= 198°C . The chemical formula is: $\text{C}_{20}\text{H}_{16}\text{FN}_3\text{O}_5$. IR: The O-H carboxylic acid is noted at 3443cm^{-1} . while NH₂ asymmetric stretching and symmetric stretching respectively is observed at 3319cm^{-1} - 3205cm^{-1} and the N-H overlap at 3205cm^{-1} . In addition to the band 3051cm^{-1} belong to C-H aromatic while 2975cm^{-1} belongs to C-H aliphatic and in 1731cm^{-1} to the carboxylic acid group. At 1668cm^{-1} which indicates the keton group. 1618cm^{-1} for the C=C , 1307cm^{-1} for the C-F and finally cm^{-1} back to C-O ²⁸. ¹H NMR (400 MHz, DMSO) δ 7.15 (d, $J = 2.1$ Hz, 3H), 7.09 (dd, $J = 8.1, 2.0$ Hz, 3H), 6.50 (d, $J = 8.1$ Hz, 3H), 5.29 (s, 7H). ¹³C NMR (101 MHz, DMSO) δ 177.22, 168.49, 165.92, 149.68, 140.62, 134.11, 121.58, 120.89, 118.74, 115.79, 113.14, 112.35 (d, $J = 22.7$ Hz), 107.97, 49.09, 36.74, 8.14 ²⁹.

The synthesis of all derivatives is shown scheme. 1 and the Fluoroquinolones generally have an enzymatic activity center that is represented by substituent of sites 3, 6 and 7. In this paper, the substituent of site 3 is stabilized by a carboxyl group. Fluorine was used to fix the six substituent, while different substituents were used at site 7 and replaced with chlorine for formation compounds A, B, C, D and E, where the hydrogen atom resulting in all amino compounds combines with chlorine atom to form HCl (minor product). The reaction was carried out without a catalyst.





Scheme 1. Synthesis of Quinolone derivatives.

***In vitro* Antibacterial Activity**

Five chemical derivatives were examined for their activity to inhibit four types of pathogenic bacteria two gram positive (*S. aureus*, *S. pyogenes*) two gram negative (*E. coli*, *K. pneumonia*). Bacterial strains were identified and supplied from well diffusion assay. An overnight culture of bacteria was inoculated in nutrient broth and the growth was monitored and adjusted to OD600 of 0.6. The bacteria broth of each type was streaked out on Mueller Hinton Agar (MHA), and a 5 mm wells were assembled on MHA plates. The wells were

filled with 200 μ l of either 250 or 500 μ g/ml from each compound, and one with solvent as a control. The plates were incubated under aerobic conditions at 37 $^{\circ}$ C for 24 hours. The inhibition zone around each well was measured in comparison to the control. Ciprofloxacin 250 μ g was used as a positive control, and the results of the inhibition zone were explained according to CLSI 2022. Where the biological activity has been tested more than once. As the bacteria were diagnosed in the laboratories of the College of Science for Women, Department of Biology

Results and discussion

Bioactivity of Compounds

The antimicrobial activity of the compounds was evaluated *in vitro*, and the results depicting bacterial growth inhibition can be observed in Fig. 1. A summary of these findings is also provided in Table.1. The antibacterial activity of compounds *in vitro* showed inhibition growth. The study's findings revealed that, when compared to the standard antibiotic ciprofloxacin³⁰, all of the tested medicines

had excellent antibacterial effects against the tested bacterial strains.

The results clearly showed that almost all compounds were effective against two Gram-negative and two Gram-positive. The zone of inhibition was arranged from 20 mm to 47 mm, except for *Escherichia coli* which exerts a pattern of resistance towards all compounds, however, the

zone of inhibition at 250 and 500 µg/ml was 30 and 33 mm, respectively.

The "in vitro" antibacterial activity of the compounds was evaluated. The results of bacterial growth inhibition are illustrated in Figs. 2-5. The results of the study showed that when compared with the standard antibiotic (ciprofloxacin), all the tested drugs had excellent antibacterial effects against the tested bacterial strains the best activity was shown by compound C against *E. coli* with an inhibition zone of 30mm and 33 mm at 250 and 500 µg/mL respectively. While compound B in *Staphylococcus aureus* has high inhibition zone of 45mm and 47mm at 250 and 500µg/mL respectively. However compound D in *Klebsiella pneumoniae* has high inhibition zone of 31mm and 35mm at 250 and 500µg/mL respectively, while in compound A for *Streptococcus pyogenes* has inhibition zone of 45mm and 47mm at 250 and 500µg/mL respectively.

Quinolone-based heterocyclic compounds act as potent antibacterial agents positive bacteria than

Gram-negative bacteria and Gram-positive bacteria. The synthesized compounds showed good results firstly, compound C showed potent activity against *E. coli* because effect NH group that increases the electron density at ortho in the benzene, hence it activates the benzene ring. Therefore, NH acts as an activating group here and compound B in *S.aureus* indicates that the presence of the carboxylate group at the meta site while compound D in *K. pneumoniae* because the amine group has an inductive effect that pulls in electrons due to the high electro negativity of the atoms. Nitrogen is bound to the ring and has an electron donor effect through the resonance effect having free electron pairs on the nitrogen atoms and finally compound A in *S. pyogenes* because the presence of the carboxylate group in the ortho site, all these factors increase the biological activity .

In conclusion, these compounds could be an alternative drug to inhibit and restrain the pathogenicity of two Gram negative and two Gram-positive pathogens.

Table1. Inhibition zone in (mm) of the synthesized compounds A-E compared with standard antibiotic ciprofloxacin against two Gram-positive and two Gram-negative bacteria.

Organisms	A		B		C		D		E		Ciprofloxacin 250 µg	Control
	250µg	500	250	500	250	500	250	500	250	500		
<i>E. coli</i>	10	15	5	10	30	33	3	9	29	30	27	-----
<i>S. aureus</i>	44	45	45	47	43	44	41	43	42	44	40	-----
<i>K. pneumoniae</i>	20	21	29	30	26	27	31	35	23	24	28	-----
<i>S.pyogenes</i>	45	47	42	43	40	43	35	38	38	39	44	-----

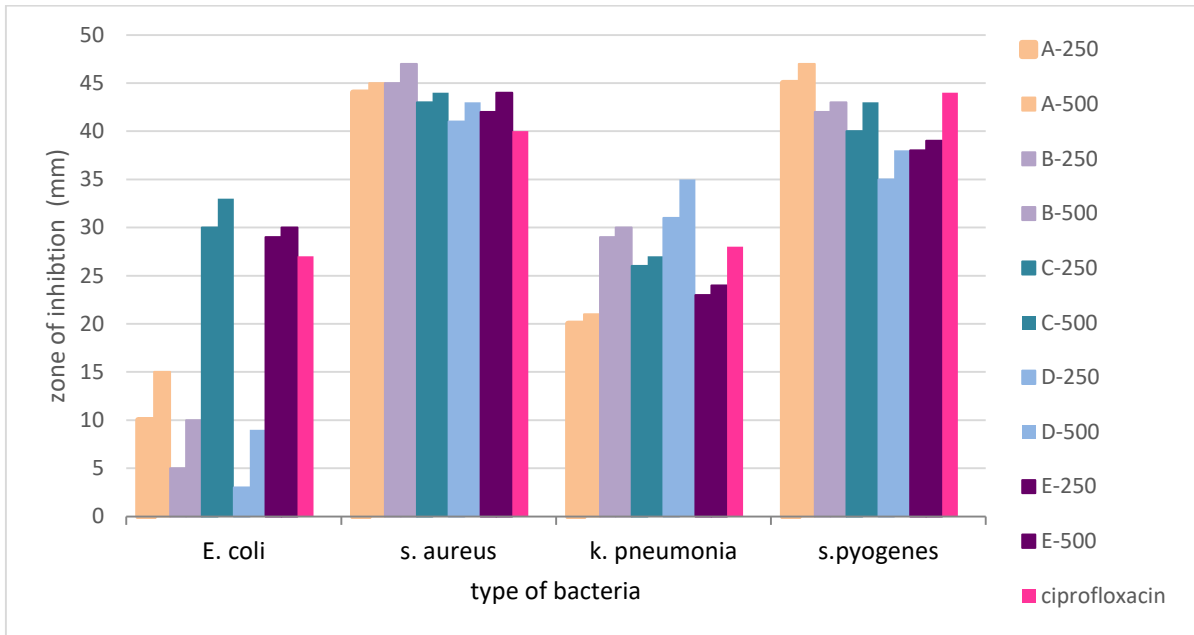
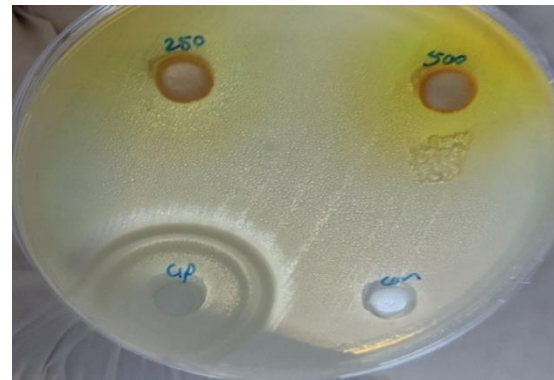


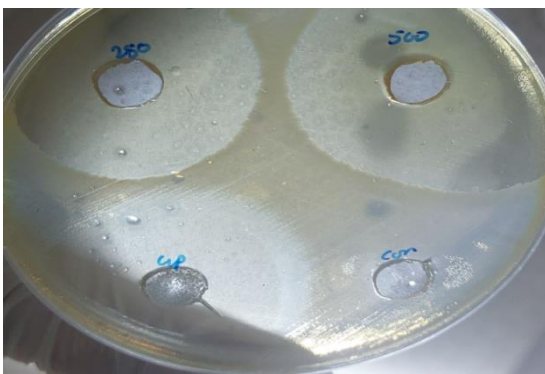
Figure 1. The inhibition zone of the synthesis compounds in mm



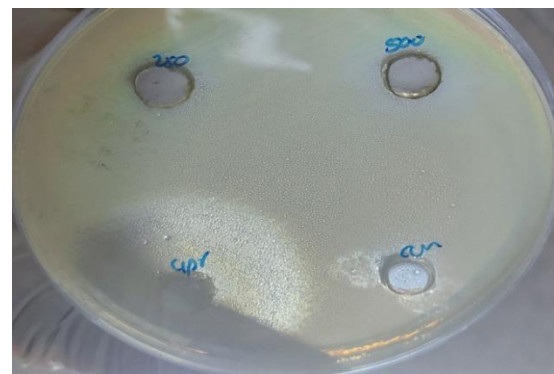
(A)



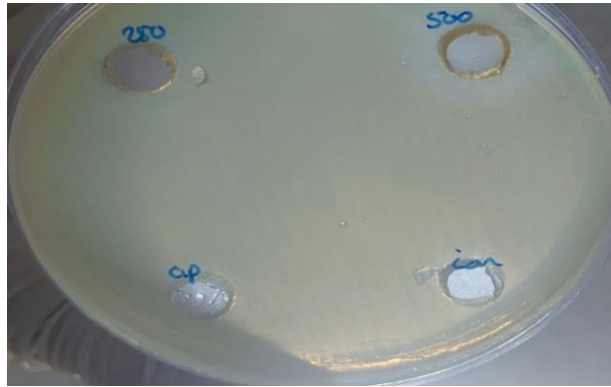
(B)



(C)

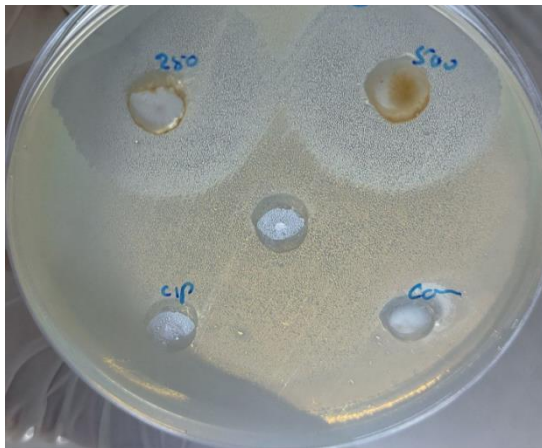


(D)

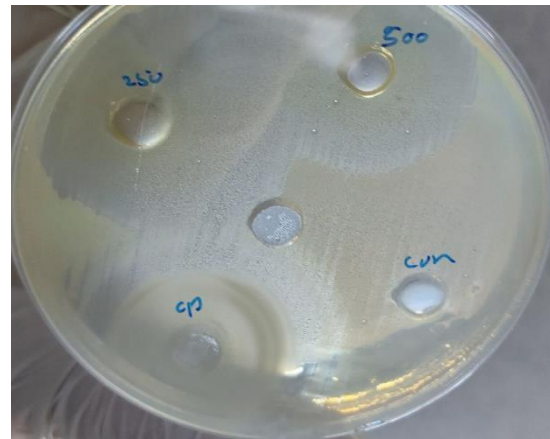


(E)

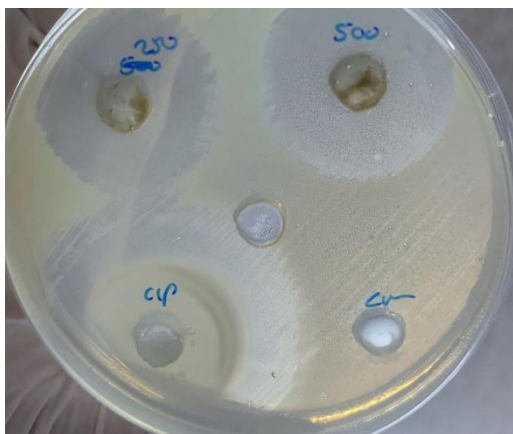
Figure 2. The antibacterial activity of compounds A-E against *E.Coli* bacterial compared to ciprofloxacin after 24 h of incubation at 37 °C



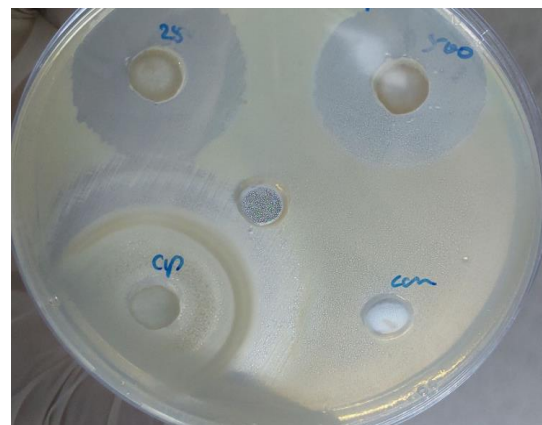
(A)



(B)



(C)

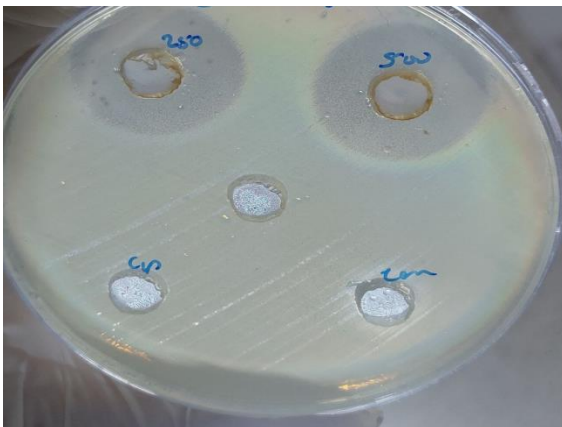


(D)



(E)

Figure 3. The antibacterial activity of compounds A-E against *Staphylococcus aureus* bacterial compared to ciprofloxacin after 24 h of incubation at 37 °C



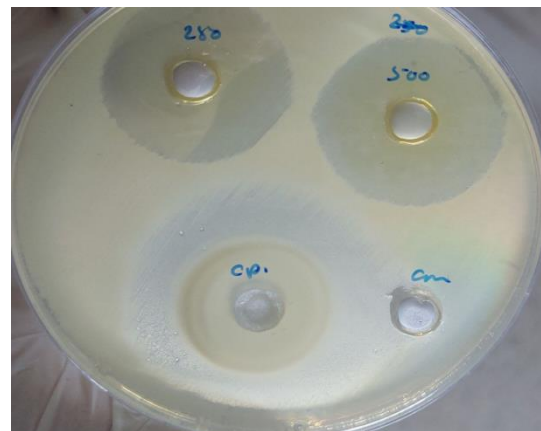
(A)



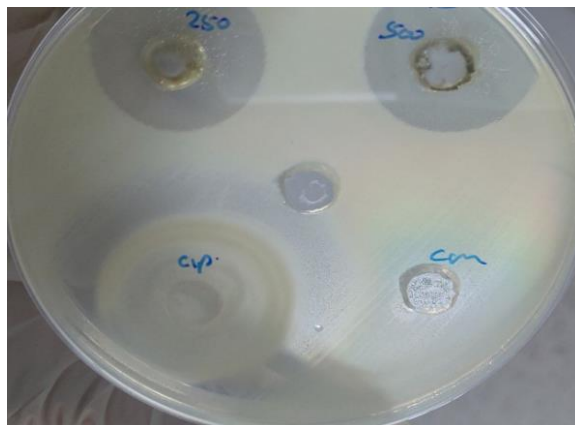
(B)



(C)



(D)



(E)

Figure 4. The antibacterial activity of compounds A-E against *Klebsiella pneumoniae* bacterial compared to ciprofloxacin after 24 h of incubation at 37 °C



(A)



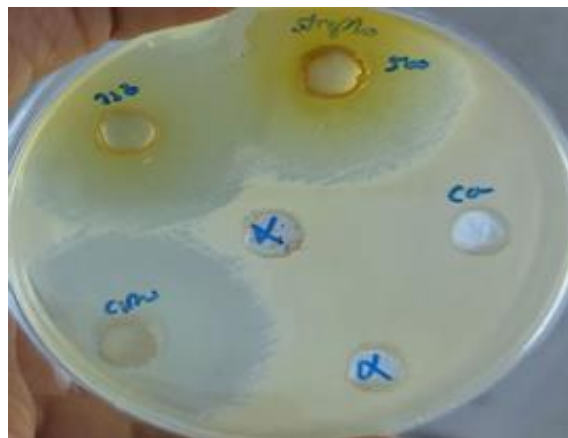
(B)



(C)



(D)



(E)

Figure 5. The antibacterial activity of compounds A-E against *Streptococcus pyogenes* bacterial compared to ciprofloxacin after 24 h of incubation at 37 °C

The FTIR results as shown in Fig. 6,7,8,9,10 and ¹HNMR, ¹³CNMR are shown in Fig. 11,12,13,14,15.

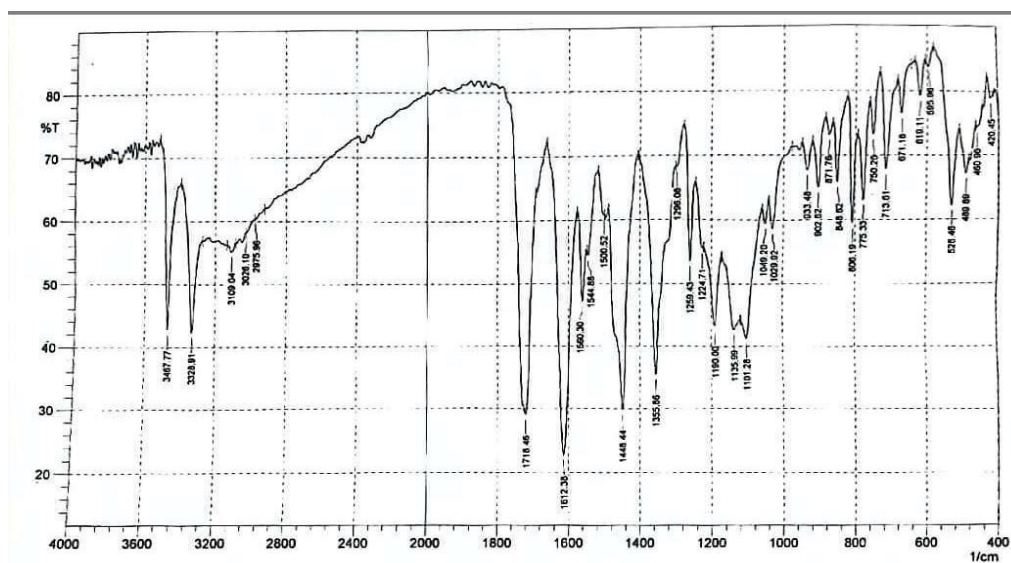


Figure 6. FTIR of Compound (A) (C₁₈H₁₃N₄O₅)

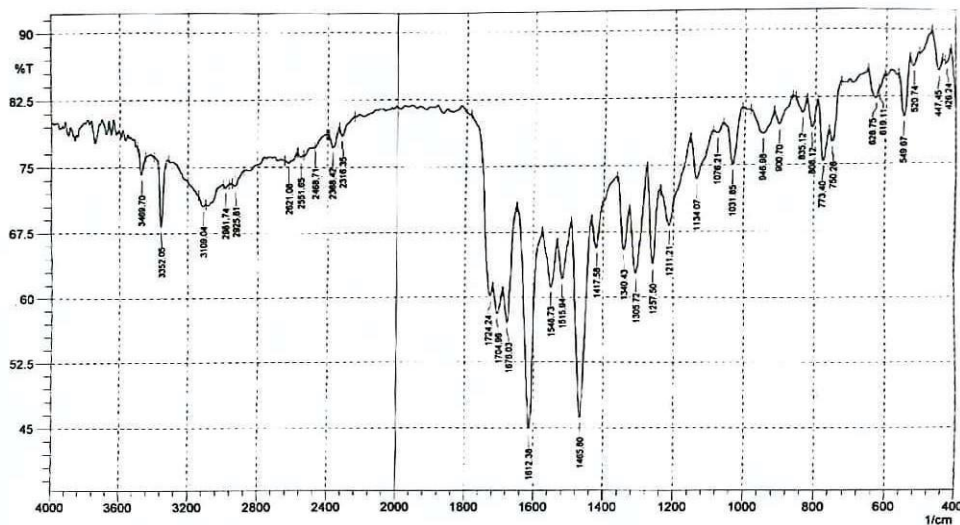


Figure 7. FTIR of Compound (B)(C₂₀H₁₅FN₂O₆)

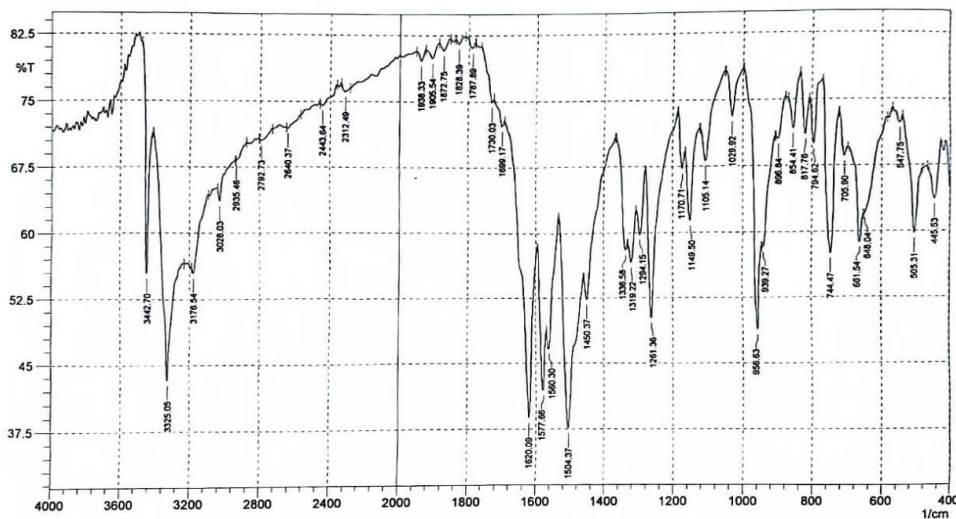


Figure 8. FTIR of Compound (C) (C₂₀H₁₇FN₄O₄)

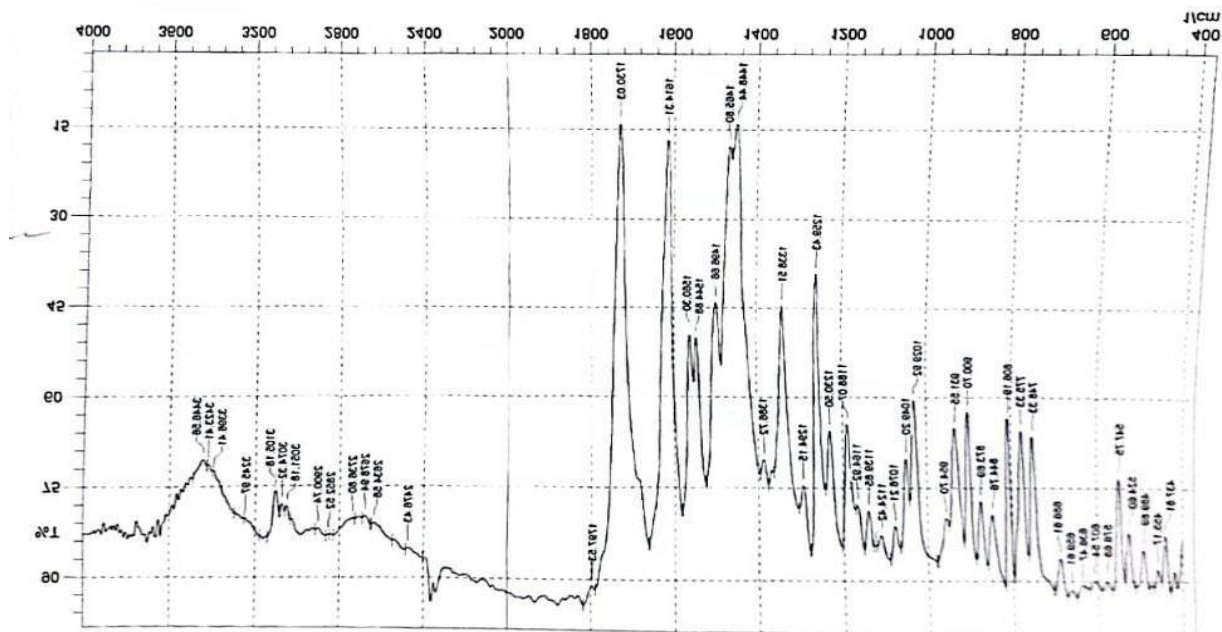
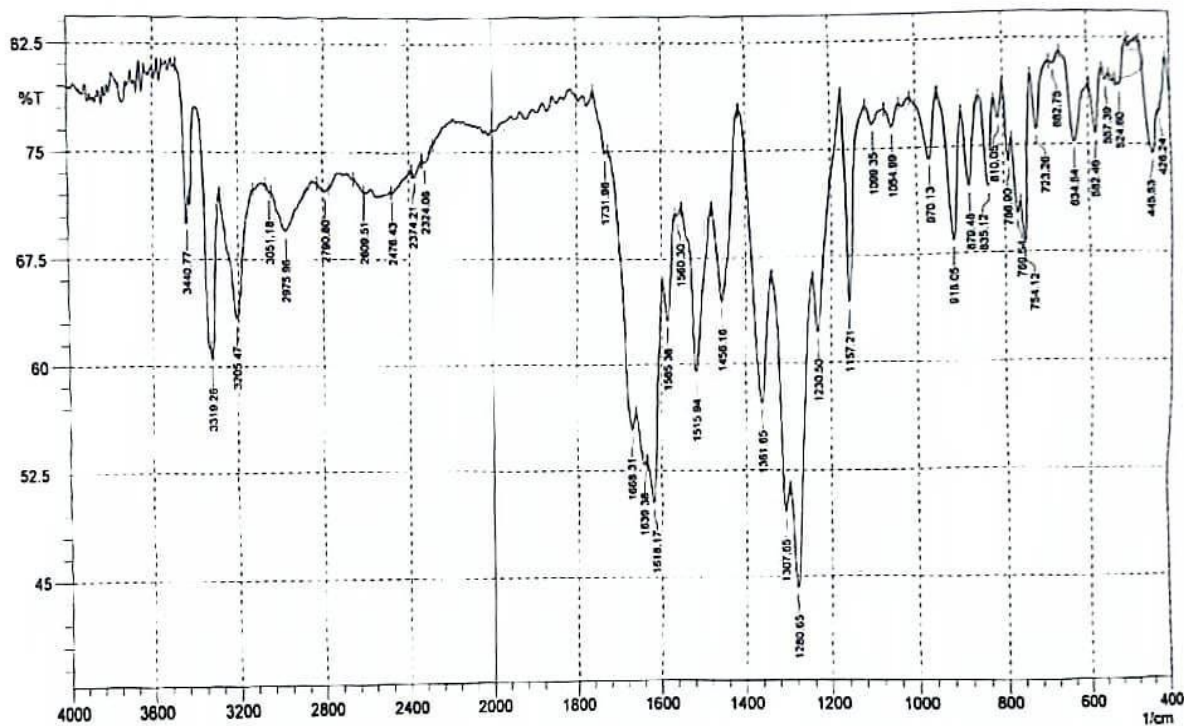
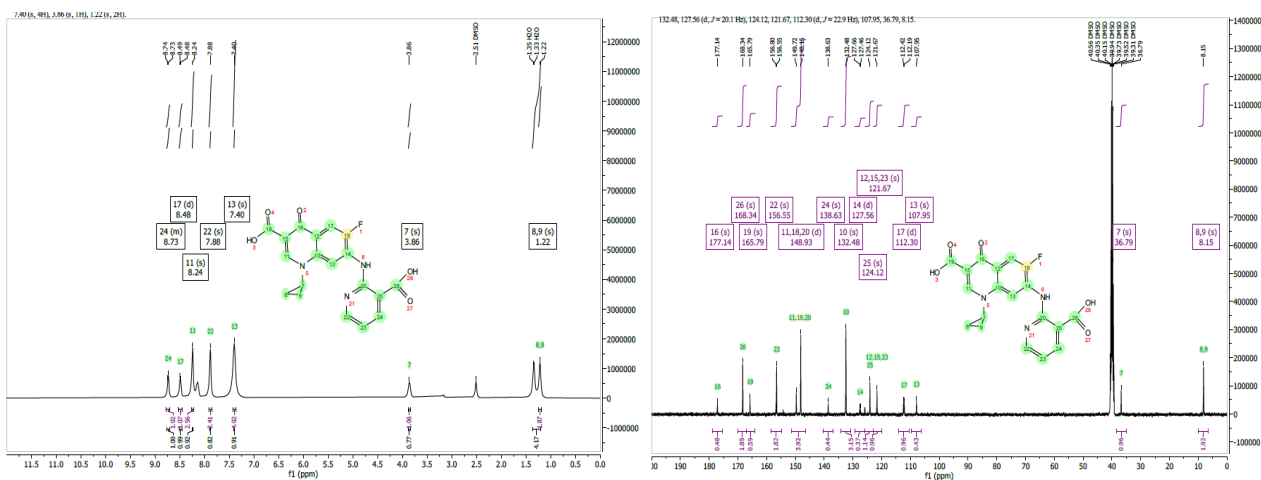
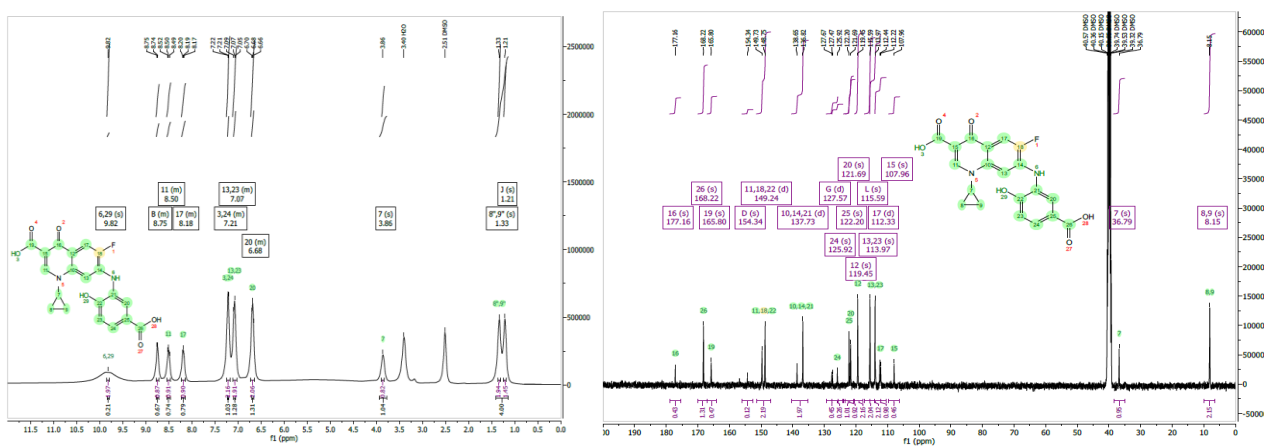


Figure 9. FTIR of Compound (D) ($\text{C}_{20}\text{H}_{18}\text{FN}_3\text{O}_3$)

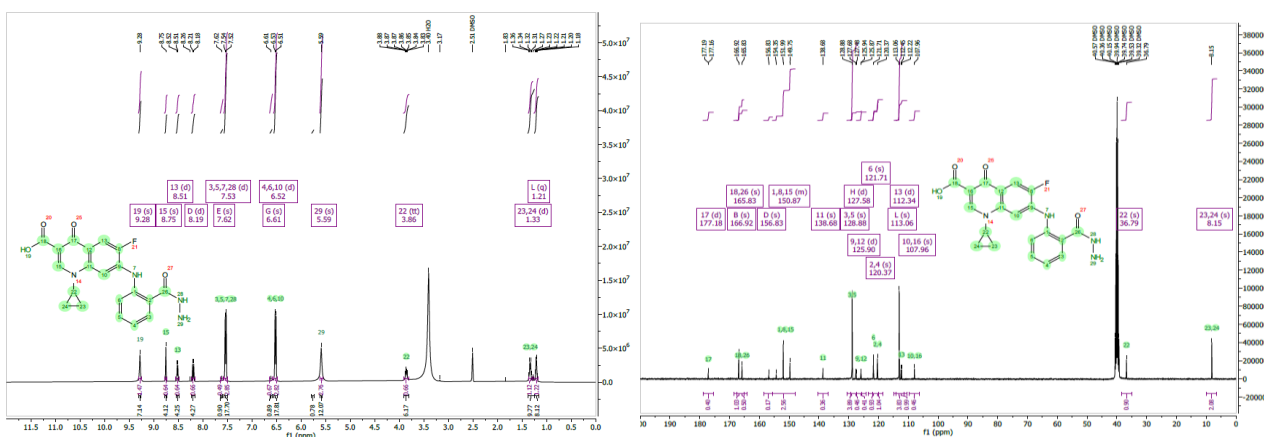




(a) (b)
Figure 11. ¹H NMR (a) and ¹³C NMR(b) of Compound A



(a) (b)
Figure 12. ¹H NMR (a) and ¹³C NMR(b) of Compound B



(a) (b)
Figure 13. ¹H NMR (a) and ¹³C NMR(b) of Compound C

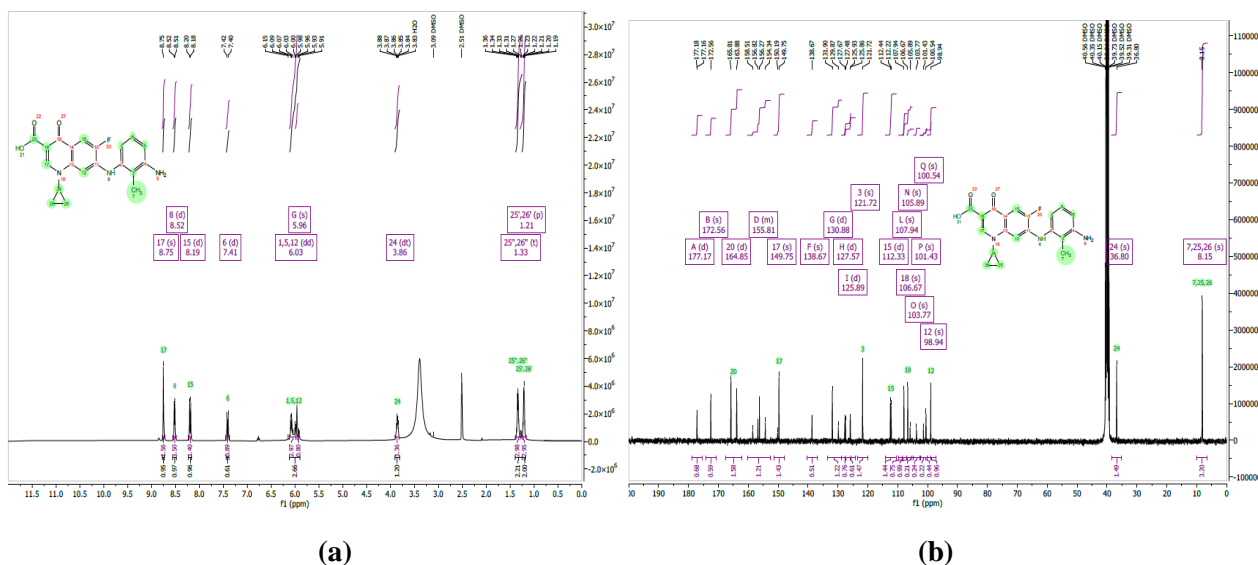


Figure 14. 1 ¹H NMR (a) and ¹³C NMR (b) of Compound D

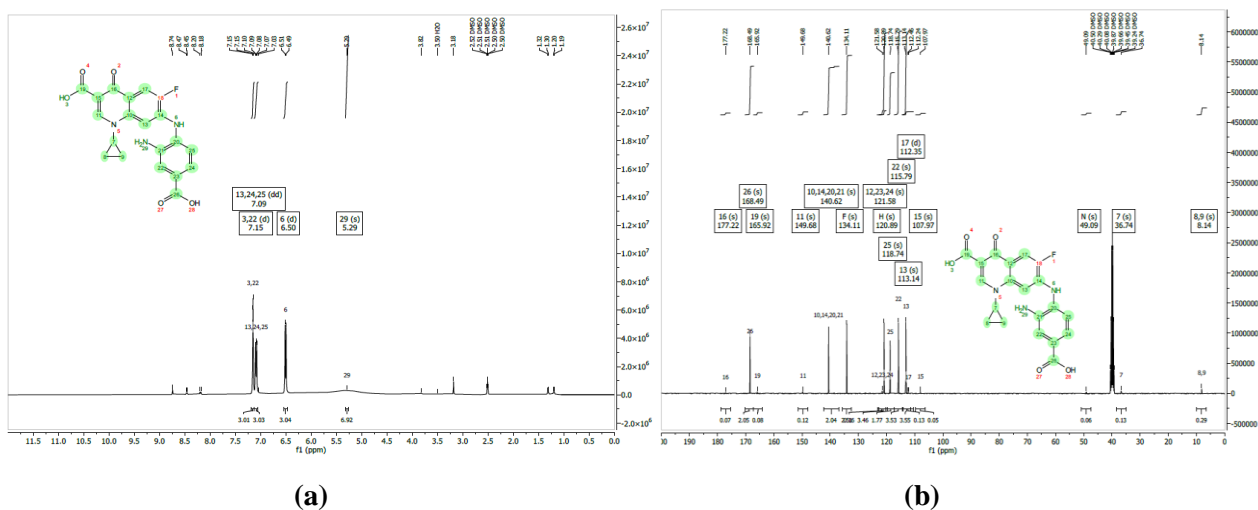


Figure 15. ¹H NMR (a) and ¹³C NMR (b) of Compound E

Conclusion

The Quinoline heterocyclic scaffold offers valuable potential for the development of bioactive compounds. In this study, we successfully synthesized a series of Quinoline derivatives. All synthesized compounds were characterized by TLC, melting point, FTIR, ¹H NMR, ¹³C NMR. Antibacterial activities of the synthesized compounds were screened by the well diffusion

assay method against two Gram-negative and two Gram-positive bacteria, and most of them were found to have efficient and accurate activities against the bacterial strains used for the screening. Compound C showed potent activity against *E. coli* and compound B in *S. aureus* while compound D in *K. pneumoniae* and compound A in *S. pyogenes*.

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Author's Declaration

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Besides, the Figures and Images, which are not ours, have

been given the permission for re-publication attached with the manuscript.

- Ethical Clearance: The project was approved by the local ethical committee at University of Baghdad.

Author's Contributions Statement

Both authors A.A.M. and A.M.F. contributed in:

- 1- Synthesis of the Quinoline derivatives and characterization by using FTIR and NMR.

- 2- Evaluation of biological activity of the synthesis compounds.
- 3- Writing and proofreading of the MS.

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تعديل جزء سيبروفلوكساسين لتحضير بعض المشتقات الجديدة مع فحص النشاط المضاد للبكتيريا

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الخلاصة

أن إحدى أكبر مشاكل الصحة العالمية هي ظهور مقاومة الميكروبية للأدوية الشائعة لذلك هناك حاجة ملحة لمضادات جرثومية جديدة ذات نشاط أحيائي معزز. في هذا الدراسة، تم تحضير خمسة مشتقات جديدة من الكينولين A, B, C, D و E كمضادات جرثومية. تم فحص بنية المركبات المحضرة باستخدام UV light , FTIR NMR . تم استخدام طريقة الانتشار بالحفر في التطبيق لاختبار الخصائص المضادة للبكتيريا للمركبات المحضرة في المختبر ضد نوعين من البكتيريا الموجبة (المكورة العنقودية الذهبية و المكورة العنقودية المقيحة) ونوعين من البكتيريا السالبة (الكلبسيلا الرئوية و البكتيريا الاشريكية القولونية). تم استخدام عقار السيبروفلوكساسين كمضاد حيوي قياسي للمقارنة مع المركبات المحضرة. تم عرض أفضل نشاط بواسطة المركب C ضد البكتيريا الاشريكية القولونية مع منطقة تثبيط تتراوح من 30مم و 33مم عند 250 و 500 مايكرو غرام على التوالي. بينما يحتوي المركب B في المكورة العنقودية الذهبية على منطقة تثبيط عالية تتراوح تبلغ 42مم و 47 مم عند 250 و 500 مايكرو غرام على التوالي. لكن المركب D في الكلبسيلا الرئوية على منطقة تثبيط عالية تبلغ 32مم و 35مم عند 250 و 500 على التوالي . بينما المركب A في المكورات العنقودية المقيحة تبلغ منطقة التثبيط 45مم و 47مم عند 250 و 500 مايكرو غرام على التوالي .

الكلمات المفتاحية: مضاد للبكتيريا ، خط الخلية ، سيبروفلوكساسين ، فحص انتشار جيد ، الكينولين.