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Original Article

Synthesis and Identification of Some New Heterocyclic Compounds for Levofloxacin Drug Derivatives with Evaluating of Their Biological Efficiency and Antioxidant Activity

Hala Shkyair Lihumis*, Zainab Abbas Al Talebi, Ahmed Kareem Khaleel

Department of Chemistry, College of science, University of Babylon, Iraq

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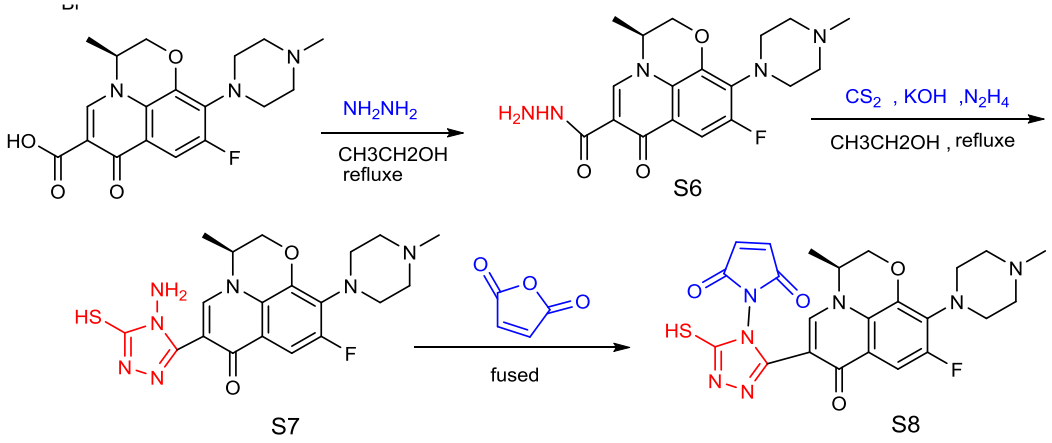
ABSTRACT

In this research study, new heterocyclic derivatives have been prepared. The most available (Levofloxacin) reacted with thionyl chloride to get acetyl chloride (S1 compound). All the synthesized compounds have been identified using FT-IR and ^{1}H-NMR spectrum. **(Scheme 1)** shows that, (S1) compound in the first line treated with thiosemecarbazide to get (S2) hydrazine carbo thio amide derivative then a ring closer reaction has been made to compound (S2) by NaOH solution to get the triazole-3-thiol ring compound (S3). Second- line compound S1 treated with amino acid (glycine) to get (S4) compound. (S5) the compound has been synthesized by reacting (S4) compound with an aromatic aldehyde in the presence of acetic anhydride to get Oxazole ring (S5 compound). Second-line compound (S) treated with hydrazine hydrate to give (S6) compound then a ring closer reaction have been made using carbon disulfide and hydrazine hydrate in basic media to get (S7). Also, (S7) compound reacted with malic anhydride to prepare triazolidine di acetic acid derivative S8 compound. Also, (S) compound treated with semecarbazide and thiosemecabazide in the presence of phosphoryl chloride ($POCl_3$) to get oxadiazole and thiadiazol containing compound respectively (S9, S10). The synthesized compounds antibacterial activity and antioxidant activity (S1-S10) were examined using the (DPPH) technique. The compounds show substantial antioxidant activity equivalent to the well-known (ascorbic acid) (IC50=31.95 g/mL) employed.

GRAPHICAL ABSTRACT



* Corresponding author: Hala Shkyair Lihumis
✉ E-mail: Email: sci.hala.shkair@uobabylon.edu.iq

Introduction

Levofloxacin is a fluoroquinolones antibiotic used to treat various infections caused by sensitive microorganisms. It is used to treat the following bacterial infections: bronchitis, Sinus infections, Urinary tract infections, pneumonia, prostatitis, skin infections, and bacterial conjunctivitis [1].

It may also be used to treat people exposed to anthrax germs or treat and prevent plague and should only be used for infections that cannot be treated with a safer antibiotic. [2]. The main side effects of this drug are nausea, abdominal pain, diarrhea or constipation, and headache [3]. It is also considered an effective bacteriostatic inhibitor that directly inhibits bacterial DNA by DNA-gyrase inhibition in susceptible organisms, Fluoroquinolones as a second line of anti-tuberculosis therapy [4]. Heterocyclic compounds are because the side groups of the most common and necessary parts of living cells are based on aromatic heterocyclic compounds. They play a crucial role in biochemical processes [5]. The presence of nitrogen and sulfur in heterogeneous rings makes it flexible to adjust and develop the drug [6]. In organic chemistry, heterocyclic compounds are widespread. Many of them have essential biological features, such as antibacterial, antifungicidal, and analgesic capabilities, as well as pharmacology, optics, and electronic material sciences. [7]. Oxazole is an aromatic heterocyclic five-membered compound and contains in their composition the oxygen atom and the nitrogen atom [8]. In 1876, the chemistry of oxazole began when preparing the 2-methyloxazole compound, while in 1962, the parent oxazole was synthesized [9]. Triazole is an organic compound containing in their structure a five-membered diunsaturated ring consisting of three nitrogen atoms and two carbon atoms at not contiguous positions. It has pair of isomeric are: 1,2,4-Triazole and1,2,3-Triazole with molecular formula$C_2H_3N_3$ [10].

Material and Methods

Experimental

After any further purification, chemicals were extracted from Merck and BDH used. Using the SMP30 melting point instrument, the melting points of the prepared compounds were determined, although the degrees of melting were not corrected. The "Testseon Shimadzu (FTIR 8400Series Japan)" with KBr disk The H^1NMR spectra were obtained with DMSO as solvent and TMS with "Bruker, Ultra Shield 500 MHZ Switzerland." as internal standard.

Synthesis of (S)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinoline-6-carbonyl chloride (S1) [11]

In 50 mL round bottom flask attached with a reflux condenser, dissolved 0.01 mol (3.61 g) of compound (S) by 50 ml of thionyl chloride. The mixture refluxed for 3 h, then the solution was concentrated by rotary and collected. The reaction was followed by TLC technique, recrystallized with absolute ethanol. Physical properties are demonstrated in (Table 1).

Synthesis of (S)-2-(9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinoline-6-carbonyl)hydrazine-1-carbothioamide (S2) [12]

0.01 mol (0.91 g) of thiosemicarbazide and 50 ml of sodium hydroxide solution (10%) are mixed with stirring for 20 min. Add a mixture of 0.01 mol (3.61 g) of compounds (S1) was dissolved in 50 mL of dioxane in a drop-wise manner over 30 min and stirred for 24 h. Then added to the iced water with stirring for 30 min acidified with concentrated hydrochloric acid. TLC was used to monitor the response. Diethyl ether was used to extract the organic layer, and the extraction was repeated four times, recrystallized with absolute ethyl alcohol (Table 1).

Synthesis of (S)-9-fluoro-6-(5-mercapto-4H-1,2,4-triazol-3-yl)-3-methyl-10-(4-methylpiperazin-1-yl)-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinolin-7-one (S3) [13]

0.01 mole (4.34g) of compound (S2) and sodium hydroxide, 4% (0.01 mole) was refluxed with stirring for 4h. Leave the mixture to cool. After that, the mixture was acidified with conc. HCl and the reaction were monitored by the TLC technique. Recrystallized with absolute ethyl alcohol (Table 1).

Synthesis of (S)-(9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4]

oxazino [2,3,4-ij]quinoline-6-carbonyl)glycine compound with 1l4,2l4-disulfene-1,2-dithione (1:1) (S4) [12]

Compounds (S3) (0.01 mol, 4.16 g) dissolved in (5 mL) of dioxane then added it to a stirring solution of glycine (0.01mol, 0.75 gm) and sodium hydroxide (10%) (20 ml). The mixture was stirred overnight, and little amounts of powder ice were added. After that, the mixture was acidified with conc. HCl and the collected solution were concentrated under a rotary evaporator device, and the reaction was monitored by TLC technique, the residual precipitate dissolved in ethanol (Table 1).

Synthesis of (S,Z)-6-(4-(4-bromobenzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinolin-7-one (S5) [14]

(4-bromobenzyldyde) 0.01 mol (1.85 g) was added to the mixture of compounds (S4) (0.01 mol, 5.46 g) and acetic acid (10 ml) and acetic anhydride (40 mL), and the mixture was refluxed for 7 h., then the mixture was added into powder ice and stirred for 0.5 h. The reaction was followed by the TLC technique, and the product was collected recrystallized with absolute ethyl alcohol (Table 1).

Synthesis of (S)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinoline-6-carbohydrazide (S6) [15, 16]

(0.01 mol, 5.66 g) of compounds (S5) was added in a round bottom flask then the mixture of hydrazine (0.01 mol, 0.32 g) and ethanol (20ml) was added. The mixture was refluxed with stirring for (5-6) h. After that, the precipitate was dried recrystallized with absolute ethyl alcohol. (Table 1).

Synthesis of (S)-6-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinolin-7-one(S7) [17]

The compound (S6) (0.01 mole, 3.75 g) and CS_2 (0.01 mole, 0.76 m) were added to potassium hydroxide (0.02 mole, 0.56 g) and ethyl alcohol (10 mL) then stirred for 12 h. Then, (20 mL) of diethyl ether was added, the resulting solid precipitate was washed with diethyl ether., and purification by dissolved in water (10 mL), then hydrazine hydrate 80% (0.02 mole, 0.32 g) was added. The mixture was refluxed for 1 h. The product cooled and diluted with water and acidified by using acetic acid. A rotary evaporator device evaporated the increase of the solvent. The reaction was monitored by the TLC technique recrystallized with absolute ethanol. (Table 1).

Synthesis of (S)-1-(3-(9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinolin-6-yl)-5-mercapto-4H-1,2,4-triazol-4-yl)-1H-pyrrole-2,5-dione (S8) [18]

(0.01 mol, 3.41 g) of S7 was fused with (0.01 mol, 0.98 g) of malic anhydride for 30 min in an oil bath after cooled ethanol was added with stirring. The reaction was followed by the TLC technique, and the product was collected. And recrystallized with absolute ethyl alcohol (Table 1).

Synthesis of (S)-6-(5-amino-1,3,4-thiadiazol-2-yl)-9-fluoro-3-methyl-10-(4-methyl piperazin-1-yl)-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinolin-7-one (S9) [19]nthesis of (S)-6-(5-amino-1,3,4-oxadiazol-2-yl)-9-fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-2,3-dihydro-7H-[1,4] oxazino [2,3,4-ij]quinolin-7-one (S10)

The compound (S) (0.01 mole, 3.61 g) was dissolved with (0.01 mole, 0.91 g, 1.11 g) thiosimecarbazide, simecarbazidehydrochioride using 10 mL of $POCl_3$ as solvent. The mixture was gently refluxed for 36 h. After cooling, added crushed ice slowly. The mixture was mixed slowly with continuous stirring. The acid mixture was mixed with potassium carbonate. The mixture was left for the next day to settle. Collect the precipitate by filtration and wash with distilled water (50 mL). The crystal is recirculated with the appropriate solvent (distilled water). TLC technique was applied to the reaction. The precipitate was filtered and recrystallized with absolute ethanol.

Table 1: Physiical properties of (S1-S10) compounds

Com. No.	Molecu. Formu.	M.W.	Color	m.p. ^{o}C	Yield%	Rf	(TLC)
S1	$C_{18}H_{19}ClFN_3O_3$	397	Brown reddish	Oil	85	-	-
S2	$C_{19}H_{23}FN_6O_3S$	434	Light brown	122-124	93	0.77	Acetone:n-hexane 1:2
S3	$C_{19}H_{21}FN_6O_2S$	416	Yellow-green	99-102	65	0.85	Petrolum ether : $CHCl_3$ 1:1
S4	$C_{20}H_{23}FN_4O_5S_4$	546	Yellow	88-92	75	0.68	n-hexane:$CHCl_3$ 1:1
S5	$C_{27}H_{24}BrFN_4O_4$	566	White	98-102	86	0.7	Ethyl acetate 3:1
S6	$C_{18}H_{22}FN_5O_3$	375	Light yellow	102-105	64	0.71	Petolum ether :$CHCl_3$ 3:3
S7	$C_{19}H_{22}FN_7O_2S$	431	Dark orange	90 -95	86	0.76	n-hexane: DCM 1: 1
S8	$C_{23}H_{22}FN_7O_4S$	511	Orange	78-79	78	0.75	n-hexane: DCM 1: 1
S9	$C_{19}H_{21}FN_6O_2S$	416	Light brown	192-195	57	0.57	Acetone: hexne 1:1
S10	$C_{19}H_{21}FN_6O_3$	400	Brown	Oil	55	0.85	Hexane:acetone 3:3

Results and Discussion

In this study, new heterocyclic derivatives of triazolidine from available and straightforward (Levofloxacin) starting materials to get heterogeneous ring compounds containing rings such as oxazole and triazole derivatives of vital importance to their similarity. Studying the applications of these derivatives were carried synthesized from. In addition, the study examined the effect and efficacy of biologic anti-two types of Gram negative bacteria (*Escherichia coli*) and positive Gram (*Staphylococcus aureus*) and antifungal (*Aspergillus Niger*) and antioxidant activity.

Synthesis and identification of compound (S1)

Compound S1 was prepared by reacting the compound (S) with thionyl chloride to produce acid chloride, HCl, and SO_2 gas (Scheme 1).

The IR spectrum of the compounds (S1) shown the structures of compounds (S1) identification by absence of the band of hydroxyl group at 3404.47 cm-^{1}, and appear new sharp band at 1788 and 752 cm^{-1}, refers to carbonyl group of acid chloride and chloride bond consecutively. Also, we can see the (CH_{ar}) at 3084 cm-^{1}, (CH_{alph}) at 2941-2873 cm^{-1}, C=C group at 1581cm^{-1}-1494 cm^{-1}, 1446 cm^{-1}-1573 cm^{-1}, C-N at 1373 cm^{-1}, at 1288 cm^{-1}-1303 cm^{-1} C-O group (Table 2).

^{1}H-NMR spectra showed disappearance singlet signal at 11.02 ppm of (COOH) and appearance singlet signal at 2.23 ppm of (C$\underline{H_3}$-N) group and appearance singlet signal at (2.31, 343) ppm of two proton of C$\underline{H_2}$-N group, and appearance singlet signal at 3.53, 4.34 ppm of protons to C$\underline{H_2}$ -O, a signal at 8.35 ppm -7.69 ppm for tow protons of the aromatic region and singlet signal at 2.11 ppm due to the proton of $\underline{CH_3}$ group (Table 3).

Synthesis and diagnosis of compound (S2)

The IR spectrum of the compound (S2) reveals the structures of compound (S2) identified respectively by the absence of absorption bands due to CO-Cl at 1788 cm^{-1}. Also, we can see the absorption band peak at 3255 cm^{-1}-3424 cm^{-1} to NH2 and absorption band peak at 3155 cm^{-1} to NH, (C-H_{ar}) at 3028 cm^{-1}, (CH_{alph}) at 2981cm^{-1}, C=C at 1537 cm^{-1}, C=O of amid group at 1595, C-N at 1369 cm^{-1}, and the absorption peak at 1103 cm^{-1}-1016cm^{-1} to (C-O) (Table 2).

^{1}H-NMR spectrum of the compounds (S2) shown appearance singlet signal at 3.57 ppm, 3.57 ppm due to proton of (C$\underline{H_2}$C=O) and signal at 7.42 ppm-8.04 ppm for ten protons of the aromatic region, doublet peak at (8.09ppm, 8.10ppm) to proton (-N$\underline{H}$), singlet peak at 8.23 ppm, to (N$\underline{H_2}$), doublet signal at 2.02 ppm to proton (S=C-N$\underline{H}$), peak at 3.47 ppm to two proton of (N-C$\underline{H_2}$), and peak at 3.02 ppm to proton (C$\underline{H\text{-}N}$), and signal at 2.13 ppm to proton to (C$\underline{H_3}$-N) (Table 3).

Synthesis and identification of compound (S3)

The cyclic closing of thiocemicarbazide derivatives in compound (S2) with (4% NaOH)

for the formation of the triazole derivative (1,2,4-triazole-3-thiol).

The IR spectrum of the compounds (S3) shown, the structures of compounds (S3) identified by appearance of absorption band at 3448-3439 cm^{-1} related to NH group and appearance of absorption band at 2279cm^{-1} to S-H, (C=C) at 1525 cm^{-1}, (CH_{alph}) at 2926 cm^{-1}, (CHar) at 3068 cm^{-1}, and appearance of absorption band at 1633 cm^{-1} to C=N, 1360 cm^{-1}, (C-N), 1211 cm^{-1}-1072 cm^{-1} to C-O (Table 2).

^{1}H-NMR spectra of compound S3 showed appearance singlet signal at 3.79ppm, 3.50ppm because of tow protons of (2N-C$\underline{H_2}$), and singlet signal at 5.02 ppm to two protons of triazolidin ring and doublet signal at 7.39 ppm- 8.10 ppm for protons of aromatic region, doublet signal at 11.48 ppm, 11.52 ppm, proton (S$\underline{H}$, N$\underline{H}_{trizol}$), and doublet signal at 3.85ppm to tow proton of NC$\underline{H_2}$ and triplet signal at 2.02 ppm to proton (N-CH) and singlet signal at 3.73 ppm to proton to (C$\underline{H_3}$-N) (Table 3).

^{13}C-NMR spectra of compounds (S3) showed appearance signal at 50.79ppm to ($\underline{C}H_2$-triazol), an appearance signal at 100.84 ppm, to (Triazolidin ring), appearance signal at 127.75 ppm-142.84 ppm to (Car), appearance signal at 160.02ppm, C-SH to (triazol ring), and signal at 50.52ppm (NH$\underline{C}H_2$), and signal at 161.95 to HN-$\underline{C}$=N and 142.77 ppm, and signal at 161.14 ppm to HN-$\underline{C}$ and 176.14 ppm to $\underline{C}$=O (Table 3).

Synthesis and diagnosis of compound (S4)

Compounds S5 have been prepared through the reaction of acid chloride of compounds (S1) with the glycine amino acid in a primary medium through the nucleophilic reaction by the electron supply in the nitrogen atom in the acid glycine on the acid carbonyl chloride

The IR spectrum of the compound (S4) reveals the structures of compounds (S4) identified by the appearance broad absorbent band of the stretch (OH) of the carboxylic group at 3433-2400 cm^{-1}. And the appearance stretching band at 3219 cm^{-1} is related to NH group. Appearance absorption band of the carbonyl group appeared at 1707 cm^{-1} and 1624 cm^{-1} was a good indication for the formation of amides carbonyl, (C=C) at 1534 cm^{-1}, (CH_{alph}) at 2924-2856 cm^{-1}, (CH ar) at 3059 cm^{-1}, 1323 cm^{-1} to (C-N) 1251 cm^{-1}-1082 cm^{-1} to (C-O) (Table 2).

^{1}H-NMR spectra of (S4) show the appearance doublet signal at (4.65 ppm, 4.41 ppm) due to protons of (HN-C$\underline{H_2}$COOH) and singlet signal at 2.05 ppm to the proton of (N-N$\underline{H}$), Singlet signal at 3.65 ppm, 3.58 ppm attributed to four protons of (N-C$\underline{H_2}$-C=O), and doublet signal at 7.34 ppm-8.15 ppm) for protons of the aromatic region, and triplet signal at 8.73 ppm, to proton (O=C-N$\underline{H}$-CH_2), and singlet signal at 11.47 ppm, to proton to (O$\underline{H}$) of hydroxyl carboxylic group, doublet signal at 3.65ppm to the proton of (NH-C$\underline{H_2}$) (Table 3).

Synthesis and diagnosis of compound (S5)

Compound S5 have been prepared by closing the ring through the reaction of the compound (S4) with an aromatic aldehyde (4-bromobenzaldehyde) in a combination of acetic acid and acetic anhydride to obtain oxazole derivatives (1.3-oxazole)

The IR spectrum of compound S5 showed disappearance of broad absorbent band of the stretch (OH) of the carboxylic group at 3433 cm^{-1}-2400 cm^{-1} of S4 and absorption band at 1525 cm^{-1} to (C=Car), absorption band at 2939 cm^{-1}-2981 cm^{-1} to (CH_{alph}), and (CH_{ar}) at 3059 cm^{-1}), and appearance of absorption band at 1755-1735 cm^{-1} to carbonyl group of ester, and 1670 cm^{-1} to C=N, 1593 cm^{-1} to C=C , 1377c m^{-1} to C-N and 1203 cm^{-1}-1246 cm^{-1} to C-O and 821cm^{-1} to C-Br, and 1558 cm^{-1}-1489 cm^{-1} to C=C ar (Table 2).

^{1}H-NMR spectra S5 showed appearance singlet and signal at 2.75 ppm, because of proton of (C$\underline{H_2}$-oxazol), and singlet signal at 5.08ppm, 5.04ppm to two protons of CH_2-O and at 7.47 ppm-7.63 ppm for protons of the aromatic region, singlet signal at 7.65ppm to proton (C$\underline{H}$=C), 3.65 ppm to proton C$\underline{H_2}$-N), and signal at 2.20ppm to proton (N-CH_3) (Table 3).

^{13}C-NMR spectra S5 showed appearance signal at 52.79 ppm, to ($\underline{C}H_2$-triazol), a signal at 103.51 ppm, 89.56 ppm (***C***H- ring), signal at 113.51ppm to (Ar***C***H=C), a signal at 123.51 ppm-135.21 ppm, (Car), signal at 131.65 ppm to (C oxazol ring), a signal at 169.07 ppm, (C=O), signal at 171.07 ppm, to(O-C=N), and signal at 168,59ppm ($\underline{C}$H=). (Table1.3).

Synthesis and Diagnosis of Compounds (S6)

The compound (S) reaction with hydrazine hydrate (80%) in absolute ethanol as a solvent to form a hydrazide derivative S6.

The IR spectrum of compound (S6) shown the absence of broad absorbent band of the stretch (OH) of the carboxylic group of S6 compound at 3448 cm^{-1}-2400 cm^{-1}. And the appearance of absorption band at 3302 cm^{-1}-3200 cm^{-1} related to NH_2 group and the stretching band at 3170 cm^{-1} related to NH group. A significant decrease in the absorption band of the carbonyl group appeared to become 1670 cm^{-1} was a good indication for the formation of amides carbonyl, (C=C) at 1573 cm-^{1}, 1604-1492 cm-^{1}, (CH_{alph}) at 2947 cm^{-1}, 2980 cm^{-1}, (CHar) at 3051 cm-^{1}, 1446 cm^{-1}, 1373 cm^{-1} to (C-N), 1211 cm^{-1} to C-O Table 3.

Synthesis and identification of compound (S7)

In cyclic reaction of S6 with carbon disulfide and potassium hydroxide as a base, then adding hydrazine (80%) in ethanol is added to form the compounds S7.

The IR spectra of compound (S7) showed a weak beak of SH absorption at 2063.83 cm^{-1}. The appearance of asymmetrical absorption band at 3317 cm^{-1}-3213 cm^{-1} related to NH_2 group, (C=C) at 1558 cm-^{1}, (C=N) at 1681 cm-^{1}, (CH_{alph}) at 2904 cm^{-1}, (CH_{ar}) at 3016 cm^{-1}, 1408 cm^{-1}, 1369 cm^{-1} (C-N). Also, appearance of the absorption band at 1666 cm^{-1} due to the (C=O) group (Table 2).

^{1}H-NMR spectra of compound (S7) showed appearance singlet signal at 5.58ppm of four protons of N$\underline{H_2}$ group, and appearance singlet signal at 3.74 ppm, 3.82 ppm because of four protons of N-C$\underline{H_2}$, and appearance singlet signal at 4.82ppm of 2 protons CH_2-O and signal at 7.21 ppm- 7.73 ppm, for protons of aromatic region and appearance singlet signal at 13.73ppm to SH_{trizol}, and doublet signal at 4.12ppm because of two proton of (C$\underline{H_2}$-NH), and appearance signal at 2.01 ppm of proton of (C$\underline{H_3}$-N), (Table 3).

^{13}C-NMR spectra of compound S7) showed appearance signal s at 51.46, 46.49 ppm to (*N*-$\underline{C}H_2$), signal at 125.90-135.89 ppm, (Car), signal at 178.34 ppm to ($\underline{C}$-SH), signal at 159.48 ppm, 149.43 ppm to (N=$\underline{C}$ -N) (Table 3).

Synthesis and identification of compound (S8)

Compound (S8) was prepared through the reaction of (S7) with maleic anhydride.

The spectral data FT-IRof compound (S8) showed the disappearance of the absorption peak due to the vibration frequency of the NH_2 group at 3317 cm^{-1}-3213 cm^{-1} and absorption peak at 3032 cm^{-1}-3062 cm^{-1} for the aromatic CH band, but absorption peak at 2974 cm^{-1}-2893 cm^{-1} for C-Haliphatic. The absorption peak of the C=C group at 1573 cm^{-1}-1604 cm^{-1} and also the appearance of a peak at 1450 cm^{-1} back to the C-N group, but the absorption peak at 1647cm^{-1} to (C=O amide) but the absorption peak at 1492cm^{-1} bake to (C-H bend) and the absorption peak at 1327 cm^{-1} - 1195 cm^{-1} to (C-O) (Table 2).

Synthesis and Identification of Compound (S9, S10)

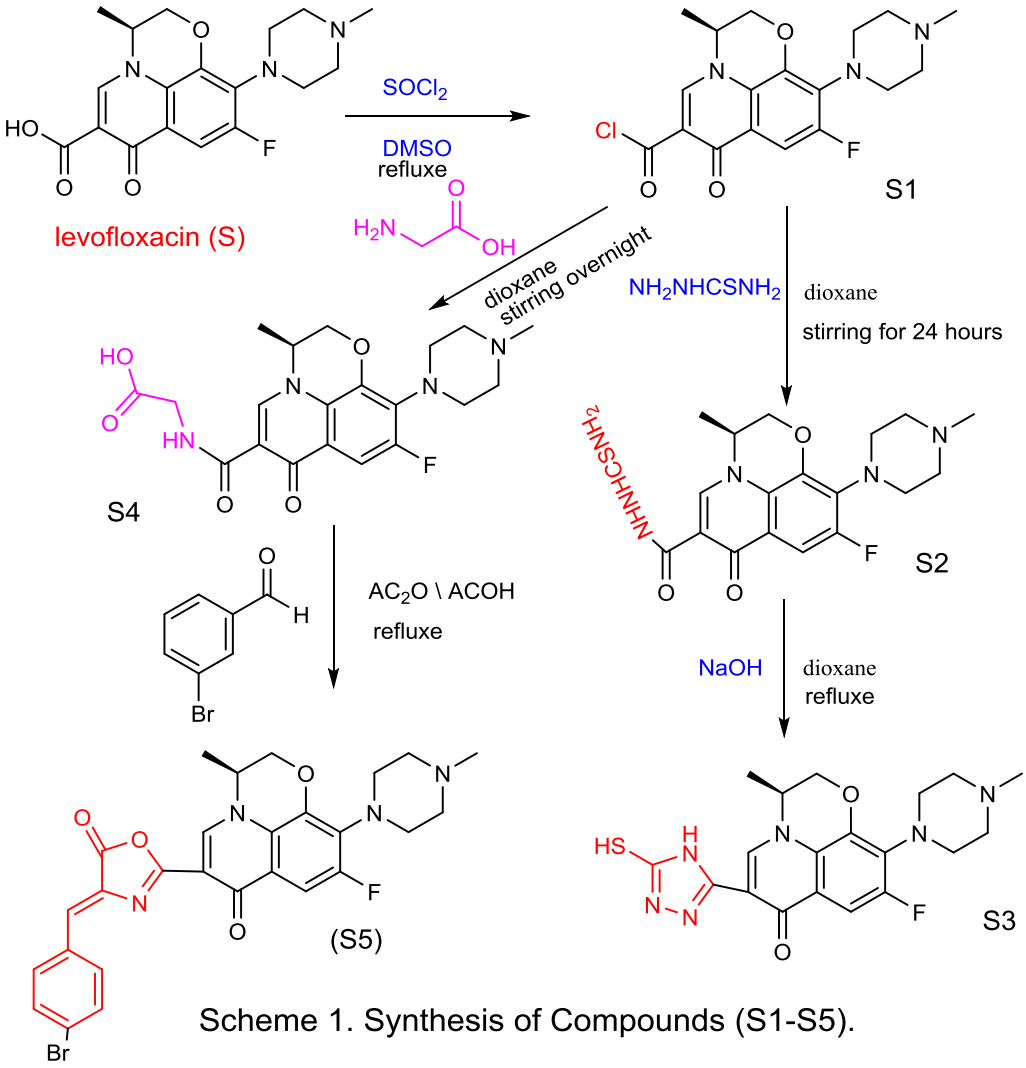
The derivatives (S9, S10) were also obtained by ring-closing reaction of the compound (S) by reacting it with the thiosemicarbazide and phosphoryl chloride.

The IR spectrum of compounds (S9, S10) showed absence peak (compound S) broad absorbent band due the stretch (OH) of the carboxylic group at 3489-2598 cm^{-1}, and appearance respectively of asymmetrical absorption band at 3423 cm^{-1}-3255 cm^{-1}, 3421 cm^{-1} -3255 cm^{-1} to NH2 and 3037 cm^{-1}, 2999 cm^{-1} to CHar and appearance of absorption band at 1610 cm^{-1}, 1605 cm^{-1} to C=N and 1535 cm^{-1}, and 1580 cm^{-1}- 1537 cm^{-1} to (C=Car) and 1376 cm^{-1}, 1375 cm^{-1} C-N, C-S at 1450 cm^{-1} and N-N (Table 2).

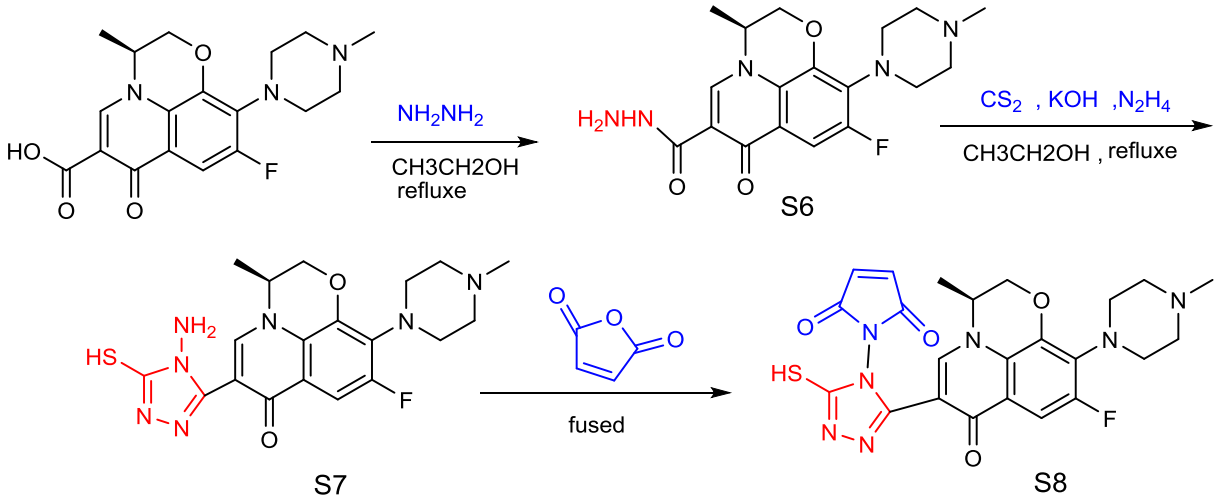
^{1}H-NMR spectra of compounds (S9, S10) showed respectively disappearance singlet signal at 10.52 ppm because of proton of hydroxyl carboxylic group (O$\underline{H}$) in (S). and appearance signal at 2.07 ppm, 2.01 ppm because proton of N-C$\underline{H_3}$ group and appearance singlet signal at 6.48 ppm, 6.49ppm because proton of N$\underline{H}$2 group and appearance singlet signal at 3.32 ppm, 3.34 ppm because of four protons of (2 N-C$\underline{H_2}$), and singlet signal at 4.94 ppm, 5.00 ppm to two protons of C$\underline{H_2}$-O, and doublet signal at 3.94ppm to two protons of NH-C$\underline{\boldsymbol{H}_2}$ and doublet signal at 7.31 ppm-7.94 ppm, 7.31 ppm-8.61 ppm, for protons of the aromatic region (Table 3).

C^{13}-NMR spectra of compound S10 showed appearance signal at 49.99 ppm, to ($\underline{\boldsymbol{C}}H_2$-NH),

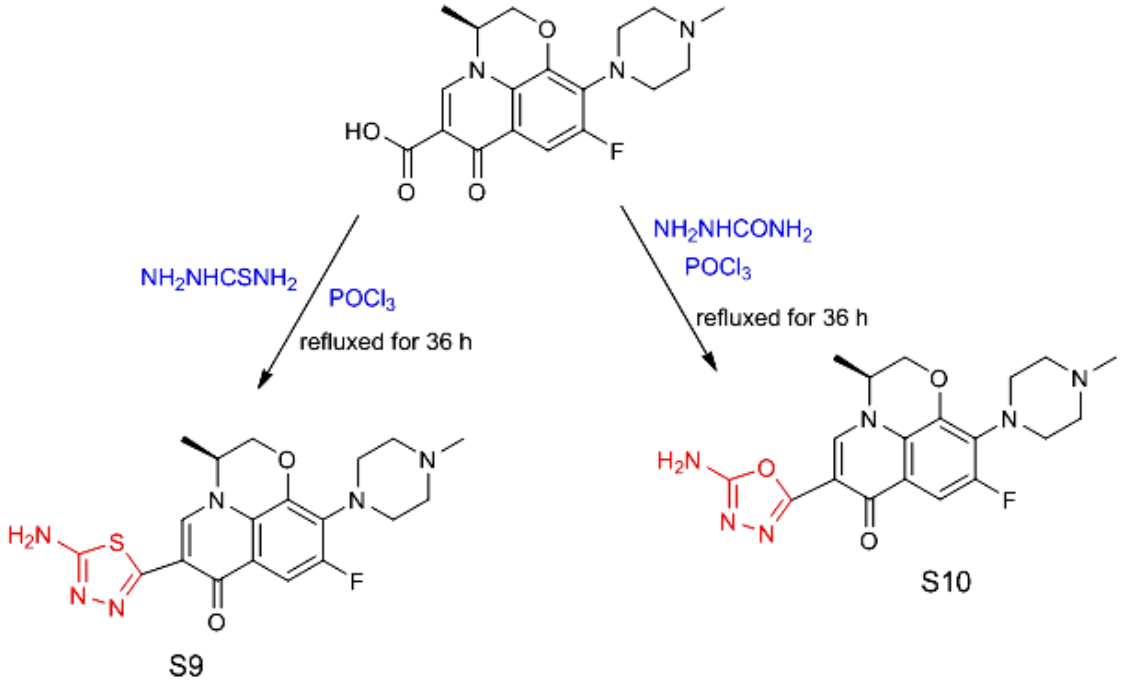
signal at 52.97ppm, to (N-**C**H_2), peak at 59.34ppm to (CH_2-O), a signal at 128.28-141.49ppm, (Car), but the signal at 161.99ppm to S-C(=N)(NH_2) , signal at 193.95 to -CH_2-C(=N)(S).



Scheme 1. Synthesis of Compounds (S1-S5).



Scheme 2: synthesis of compound (S6-S8)



Scheme 3: synthesis of compound (S9-S10)

Table 2: FT-IR bands of compounds (S1-S10)

Com. No.	IR (KBr) ν cm^{-1}								
	υ CH_{ar}	υ CH_{aliph}	υ NH	υ C=O	υ OH acid	υ C-N υ C=O $_{acid}$	υ C-O	υC=C_{ar}	others
S1	3084	2941	2835 2775	1788 1680	-	1373	1288	1581-1494	
S2	3028	2981	3155	1595 1682	-	1369	1287, 1103	1537	υ NH2:3255
S3	3068	2926	-	1697	-	1360	1211	1525	υSH:2279 υC=N:1633
S4	3059	2924	3219	1707 1624	**3433-2400**	1323	1251	1534	-
S5	3059	2939	3219	**1755 1735 1670**	-	1377	1203	1525	υC=N:1637 υC-Br:821
S6	3051	**2947, 2980**	3170	**1670**	-	**1446, 1373**	1211	**1604-1492**	υ NH2:3302-3200
S7	3016	2904	-	**1681**	-	**1369**	1252	1558	υSH:2063 υNH2:3317-3213 υC=N:1666
S8	**3032, 3062**	**2974, 2893**	-	**1647**	-	1450	**1327-1195**	1573	-
S9	3037	2985	-	**1679**	-	**1376, 1375**	1287	1535	υ NH2:3423-3255 υC=N:1610 υN-N: 1450
S10	2999	2989	-	**1650**	-	**1375**	1296-1212	**1580 - 1537**	υ NH2:3421-3255 υC=N:1589 υN-N: 1450

Table 3: Spectroscopy of compounds (S1-S10)

Com. No.	NMR (δ ppm)
S1	^{1}HNMR (δ ppm): 8.53-7.69 (2 H, Ar), 2.23 (s, 3H, C*H*$_3$-N), 3.53, 4.34 (s, 2H, CH$_2$-O), 2.31,343 (d, 2H, CH$_2$-N), 2.11(s, 3H, CH$_3$), 5.31.
S2	^{1}HNMR (δ ppm): 7.09-7.69 (10 H, Ar), 2.13 (s, 3H, C*H*$_3$-N), 3.57(s, 2H, CH$_2$ C=O), 3.47 (d, 2H, CH$_2$-N), 8.09 (s, 1H, NH), 8.23 (s, 1H, NH), 2.02 (S=C-N*H*).3.02 (C*H-N*).
S3	^{1}HNMR (δ ppm): 7.93-8.10 (Ar), 11.48, 11.52 (s, 1H, S*H*, N*H*$_{trizol}$), 3.79, 3.50 (2N-CH$_2$-), 5.02 (s, 2H, triazolidin ring), 3.85(NC*H*$_2$), 3.73 (3H, CH$_3$-N), 2.02 (s, 1H, N-CH). ^{13}CNMR (δ ppm): 50.79 (*C*H$_2$-triazol), 161.95 (HN-*C*=N), 142.77, 161.14 (HN-*C*), 176.14 (*C*=O), 160.02, C-SH (triazol ring), 50.52 (NH*C*H$_2$), 127.75-142.84 (Car).
S4	^{1}HNMR (δ ppm): 7.73-8.15 (H, Ar), 4.65, 4.41 (HN-C*H*$_2$COOH), 2.05 (s, 1H, N-NH), 3.65, 3.58 (s, 4H, N-CH$_2$ C=O), 8.73 (S, 1H, O=C-N*H*-CH$_2$), 11.47 (s, 1H, OH), 3.65 (s, 2H, NH-CH$_2$).
S5	^{1}HNMR (δ ppm): 7.47-7.63 (H, Ar), 2.75(S, 2H, C*H*$_2$-oxazol), 5.08, 5.04 (CH$_2$-O), 7.65 (S, 1H, C*H*=C), 3.65 (C*H*$_2$-N), 2.20 (N-CH$_3$). ^{13}CNMR (δ ppm): 52.79 (*C*H$_2$-triazol), 103.51, 89.56 (*C*H-ring), 113.51(Ar*C*H=C), 123.51-135.21, (Car), 131.65 (C oxaazol ring), 169.07, (C=O), 171.07ppm, to (O-C=N), 168, 59 (*C*H=) .
S7	^{1}HNMR (δ ppm) : 5.58(N*H*$_2$) ,3.74, 3.82 (N-C*H*$_2$), 4.82 (CH$_2$-O) , 7.21-7.73 (H, Ar), 13.73 (SH$_{trizol}$), 4.12 (C*H*$_2$-NH) , 2.01 (C*H*$_3$-N) ^{13}CNMR (δ ppm): 51.46, 46.49 (N-*C*H$_2$), 125.90-135.89, (Car), 178.34 (*C*-SH), 159.48, 149.43 (N=*C*-N).
S9	^{1}HNMR (δ ppm): 2.07 (N-C*H*$_3$), 6.48 (N*H*$_2$), 3.32 (2 N-C*H*$_2$), 4.94 (C*H*$_2$-O), 3.94 (NH-C*H*$_2$), 7.31-7.94, (H, Ar).
S10	^{1}HNMR (δ ppm): 2.01(N-C*H*$_3$), 6.49(N*H*$_2$), 3.34 (2 N-C*H*$_2$), 5.00(C*H*$_2$-O), 3.93 (NH-C*H*$_2$), 7.31-8.61, (H, Ar). ^{13}CNMR (δ ppm): 49.99 (*C*H$_2$-NH), 52.97 (N-*C*H$_2$), 59.34 (CH$_2$-O), 128.28-141.49 (Car), 161.99 (S-C=N), 193.95(CH$_2$-C=N).

Biological Efficiency

The effect and efficacy of bacteriophage antibodies against two types of bacteria (Escherichia coli) and (Staphylococcus aureus) were studied. Some of these compounds showed an antagonistic effect. It was found that the derivatives (S1, S4, S5, S6, S7, S9, S10) have high effectiveness in inhibiting the growth of negative bacteria type (*Escherichia coli*). It was also found that the compounds (S1, S2, S3, S5, S6, S7, S8) have high effectiveness in inhibiting bacteria (*Staphylococcus aureus*) compared to the biological effectiveness of cefotaxime, as shown in Table 1.4.

Table 4: Shows the inhibition of the growth of the bacteria (Inhibion Zone) by some derivatives recorded in millimeter unit

Comp. No.	***Escherichia coli***	***Staphylococcus aureus***
Cefotaxime (Antibiotic) Standard	**11**	**16**
S1	**15**	20
S2	**9**	25
S3	8	20
S4	14	15
S5	15	12
S6	**30**	25
S7	12	27
S8	7	19
S9	16	11
S10	19	13

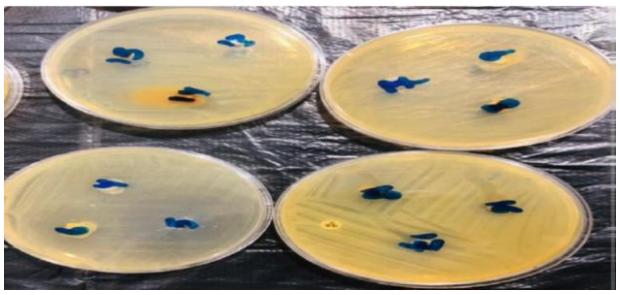


Figure 1: Biological Effect of compounds

Ant-oxidant activity

Compounds antiradical operation was performed using the standard DPPH method [20].

DPPH (1.3 mg/mL) was produced as a standard solution in MeOH, and 100 µL DPPH was added to 3 mL MeOH to measure absorbance at 517 nm.

The concentrations of the different compounds (25, 50, 75, and 100 g/mL) were prepared. 1 mL of the material was diluted to 3 mL with 100 mL of DPPH.

Tubes were exposed to light for 30 min to complete the reaction. After 30 minutes, the absorbance of each test tube was measured at 517 nm on the "UV-VIS spectrophotometer" to avoid using methanol as a blank. By drawing a line between concentration and percent inhibition, an IC50 value may be generated. Figure 2 and Table 5. Compared to normal (ascorbic acid) activity (IC50=31.95 g/mL), most compounds showed moderate to high antioxidant activity. The maximum activity was attributable to the OH group in compounds (S1-S10) with significant activity. Ascorbic acid, a generic medication, with an IC50 of 31.95 M. The forces for the antioxidant activity of the test substances are in the following order when compared to the reference: ascorbic acid (S3>S8>S2>S10 >S9>S5>S1>S7>S4>S6).

Table 5: Antioxidant activity of synthesized compounds

conc. µg\ml	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	STD (Ascorbic acid)
25	47.76	48.41	50.34	40.44	45.35	39.42	37.24	47.76	49.41	51.34	46.12
50	49.83	57.42	57.21	52.25	58.22	45.63	56.52	49.83	57.42	58.21	60.14
75	53.77	60.26	66.23	62.32	62.16	58.73	63.7	53.77	62.26	64.23	65.01
100	65.21	69.44	72.11	69.65	68.18	65.22	70.81	65.21	67.44	71.11	78.3
IC50 µg\ml	44.09	28.82	23.91	46.72	33.24	56.28	46.11	25.26	32.27	31.83	31.95

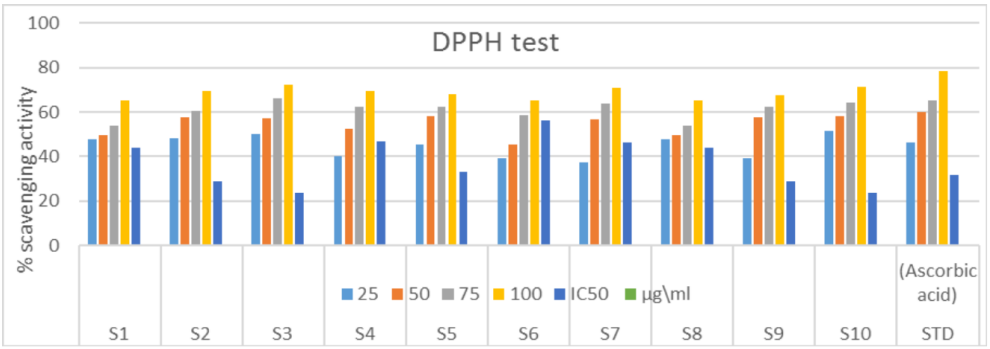


Figure 2: Graph showing DPPH scavenging activity of compounds (S1-S10)

Conclusions

In this work, new derivatives were prepared from the Levofloxacin with thionylchloride may be used to synthesize other derivatives due to having effective aggregates. The proportion of the productions was excellent and useful for

continuing the subsequent step. It is worth noting that the compounds have substantial antioxidant and antibacterial properties based on their antioxidant activity.

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Authors' contributions
All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

Conflict of Interest
We have no conflicts of interest to disclose.

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