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*Review*
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# Antibacterial Properties of Quinoline Derivatives: A Mini-Review

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**Abstract:** Antibacterial resistance plays a serious risk to human health throughout the globe. Various labors have been adopted to fight this resistance, so it is essential to design and synthesize new agents for the treatment of multi-resistance pathogens. Quinolines and their derivatives are used as antibacterial properties against various gram-positive and negative bacteria. In this mini-review, wish to report the antibacterial properties of quinoline derivatives against various pathogens in the years 2019 and 2020.

**Keywords:** quinoline; anti-bacteria; MIC; pathogens; strains; gram-positive; gram-negative.



## 1. Introduction

Quinoline is a class of natural mixtures of the aromatic heterocyclic series described by a two-fold ring structure made out of benzene and a pyridine ring melded at two nearby carbon atoms, as shown in figure 1 [1, 2]. The benzene ring contains six carbon molecules, while the pyridine ring contains five carbon atoms and a nitrogen particle. Quinoline is a frail tertiary base. It can frame salt with acids and presentations responses like those of pyridine and benzene [3, 4]. It shows both electrophilic and nucleophilic replacement responses. It is harmless to people on oral retention and inhalation. The least complex individual from the quinoline family is quinoline itself, a compound with the sub-atomic construction $C_9H_7N$. Quinoline is utilized mainly to produce nicotinic corrosive, which forestalls pellagra in people and different synthetic compounds. A few techniques are known for their synthesis, and the creation of engineered quinoline surpasses that of coal tar [5, 6].

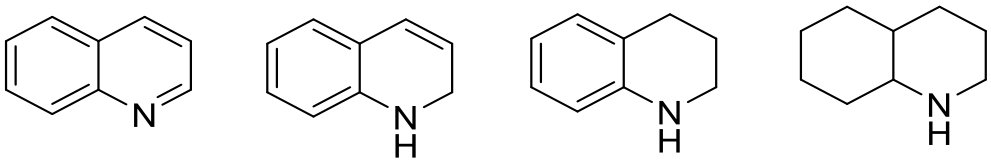


**Figure 1.** Quinoline and its reduced forms.

Quinoline core happens in a few regular mixtures (Cinchona Alkaloids) and pharmacologically dynamic substances showing a wide scope of organic action. Quinoline has been found to have antimalarial, anticancer, antibacterial, antiviral, antifungal, anti-inflammatory, analgesic, cardiovascular, central nervous system, hypoglycemic, and miscellaneous activities [7-12]. Quinoline and its combined heterocyclic subsidiaries tried with assorted pharmacological action establish a significant class of mixtures for new medication

advancement. Subsequently, numerous analysts have integrated these mixtures as target structures and assessed their organic exercises. Among heterocyclic mixtures, quinoline is a special framework that shows up as a significant development theme for the advancement of new medications [13-16].

Quinoline core is blessed with an assortment of restorative exercises, and new quinolone subsidiaries are known to be organically dynamic mixtures having a few pharmacological exercises. Numerous new restorative specialists have been created by utilizing quinoline core. Thus, quinoline and it's anything but a significant class of heterocyclic mixtures for the new medication advancement [17-19]. The antibacterial action of an atom is totally connected with the builds that commonly kill microorganisms and infection or hinder their pace of development without being widely harmful to close tissues. Most of the found antimicrobial specialists are altered normal mixtures, and this adjustment is made through a substance mode, for instance, b-lactams (penicillins), carbapenems, or cephalosporin. Unadulterated regular items, such as aminoglycosides, and other engineered antimicrobials, such as sulfonamides, are additionally habitually utilized [20-24]. The antimicrobial specialists could be delegated the specialists that can either be bactericidal, which kills microscopic organisms, or bacteriostatic, which hinders microbes' development. Antibacterial specialists are the most significant in battling irresistible sicknesses. In any case, with their wide use just as misuse, the presence of bacterial obstruction toward antibacterial specialists has become a significant issue for the present drug industry [25-27].

Antibacterial or antimicrobial activity treatment has been tested due to the disturbing rate in the ascent of contaminations brought about by microbes combined with their protection from the vast majority of first-line anti-toxin experts. This is a genuine threat to human safety and critically calls for proceeding with examination to discover compounds having better antimicrobial properties with expansive range exercises. Thus, planning new medications to treat sickness and irritations without causing huge results on patients is vital. Taking this into account, quinoline subordinates are among significant mixtures recently answered to have a wide variety of natural exercises. Along these lines, the presentation of various useful gatherings on the quinoline platform is an excellent idea for advancing new medication [28-31]. In spite of the huge advances in antimicrobial treatment achieved over the most recent couple of many years, irresistible illnesses brought about by microorganisms (microbes, parasites, infections, Mycobacterium tuberculosis, and so forth) address genuinely undermine current medication and worldwide general wellbeing. Medication opposition, multi-drug obstruction, and, broadly drug obstruction are the main source of these downsides, yet some different causes could be additionally contemplated. Quinoline-based mixtures are little atoms of colossal significance according to the pharmacological perspective, having a wide scope of natural exercises, for example, antiplasmodial and antimalarial, antibacterial or antimicrobial activity, antifungal, antitubercular, hostile to HIV, antiviral (counting against COVID-19), and so on [32, 33].

Among grouped classes of heterocyclic particles, quinoline containing strengthens stands separated as huge molecules showing a wide scope of compound, physical and natural activities. Direct quinoline subordinates are applied in the creation of tones, paints, creepy-crawly showers, and antifungals. They are furthermore used as solvents for the extraction of saps and terpenes and as disintegration inhibitors. The quinoline ring is moreover a key fundamental unit for different normal things and supported systems in therapeutic science. A quinoline center is generally present in endless designed and customary particles with

significant parasite advancement block properties. As of now, quinoline auxiliaries are available as antibacterial or antimicrobial activity (ciprofloxacin, sparfloxacin, gatifloxacin, etc.) or anticancer prescriptions (camptothecin, irinotecan, topotecan, etc.). Here in this paper, we have discussed such quinolone-based derivatives, which may provide antibacterial or antimicrobial activity aid to current medicinal or pharmacological activity [34-37].

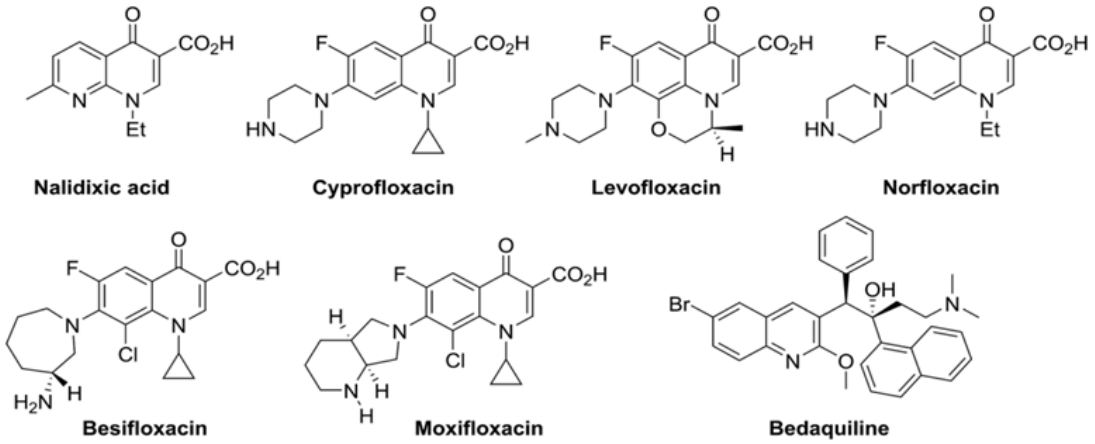



**Figure 2.** Quinoline derivatives used as potent applications (I-VII).

## 2. Results and Discussion

There are many examples of quinoline and its derivative that could be used as antibacterial drug molecules [38]. Those molecules continue to provide a trend to understand the inherent paths and suggest their possible applications in biology. This section is ardent to the utility of quinoline derivatives used as antibacterial properties against various strains; quinoline and its derivatives play a tremendous role in the pharmaceutical industry. It is well known that quinolone derivatives are used as potent drugs for various diseases.

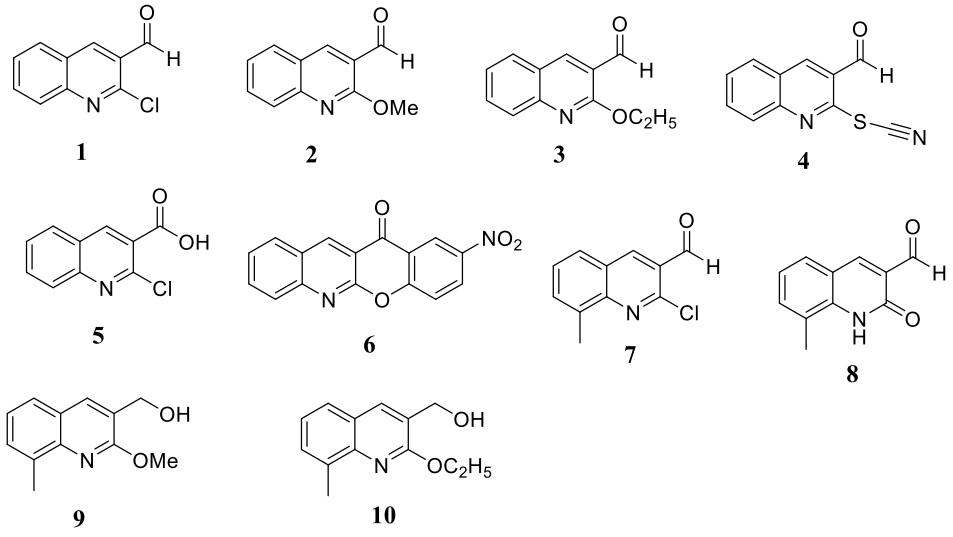
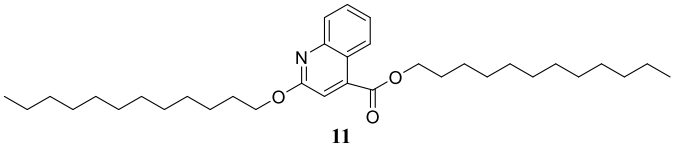



**Figure 3.** Quinoline derivatives used as an antibacterial drugs.

Quinoline derivatives are used as antibacterial properties of various gram-positive and negative bacteria and pathogens [39]. In this regard, Melaku *et al*. reported a series of quinolone derivatives (1-10) (Figure 3) and examined their antibacterial properties against various bacteria and pathogens. The antibacterial activity of the synthesized compounds was screened against gram-positive bacteria like *Bacillus subtilis* (ATCC6633) and *Staphylococcus aureus* (ATCC25923) and gram-negative bacteria like *Escherichia coli* (ATCC 25922) and

*Pseudomonas aeruginosa* (ATCC 27853). However, ciprofloxacin is used as a reference drug. From the antibacterial experiment, it is observed that all most all the derivatives show moderate to good antibacterial activity against at least two strains. The derivatives 3 and 8 exhibited excellent antibacterial activity against *Pseudomonas aeruginosa* with mean inhibition zone values in the range of 9.67 and 10.00 mm. On the other hand, derivative 5 showed potent antibacterial activity against *Escherichia coli* with a mean inhibition value of 9.00 mm compared to other derivatives [40].

The novel quinoline derivatives shown in Figure 4 [11, 12] were employed for their *in vitro* antibacterial activity against *E. coli*, *P. aeruginosa*, *S. aureus*, and *S. faecails* using the agar dilution method. Chloramphenicol and Ampicillin are used as reference drug molecules. Both compounds showed moderate to high antibacterial activity against different pathogens. The derivative 11 exhibited better antibacterial activity as compared to 12 against *S. aureus* with a MIC value of 6.25 µg/ml, which is better than the references drug molecule. However, 12 showed better antibacterial activity against *E. coli*, comparable to Chloramphenicol [41].



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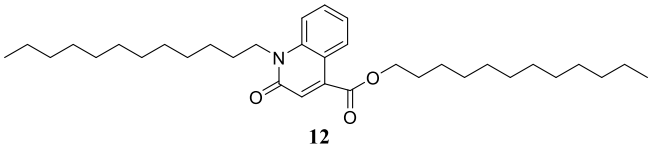

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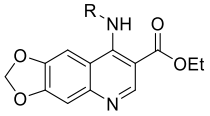
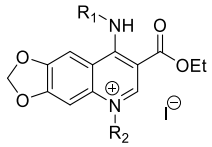




**13, R = -$CH_2$Ph**
**14, R = -$CH_2CH_2$Ph**
**15, R = -$CH_2CH_2$Ph $(OCH_3)_2$**
**16, R = -$PhOCH_2$Ph**

**17, R1 = -$CH_2$Ph; R2 = -$CH_2CH_3$**
**18, R = -$CH_2CH_2$Ph; R2 = -$CH_2CH_3$**
**19, R = -$CH_2CH_2$Ph $(OCH_3)_2$ ;R2 = -$CH_2CH_3$**
**20, R = -$PhOCH_2$Ph; R2 = -$CH_2CH_3$**

**21, R1 = -$CH_2$Ph; R2 = -$CH(CH_3)_2$**
**22, R = -$CH_2CH_2$Ph; R2 = -$CH(CH_3)_2$**
**23, R = -$CH_2CH_2$Ph $(OCH_3)_2$ ; R2 = -$CH(CH_3)_2$**
**24, R = -$PhOCH_2$Ph; R2 = -$CH(CH_3)_2$**

**Figure 4.** Quinoline derivatives used as an antibacterial drugs.

A series of quinolone derivatives (13-24, Figure 4) designed and evaluated their antibacterial activity against two human bacterial strains. From the antibacterial experiment, it is observed that all the synthesized derivatives show significant activity. On the other hand, compound 24 showed excellent antibacterial activity against *E. coli* and *S. aureus* with a MIC value of 3.125 µg/ml. The MIC value is much smaller than the references drug molecule such as amoxicillin and ciprofloxacin [42]. Ammar *et al*. reported a bunch of hybrids of quinolone and thiazole derivatives (25-28 a-f, Figure 5). The antibacterial activity was examined by using various gram-positive bacteria by using the agar diffusion method. All the synthesized derivatives showed moderate to better activity against various strains. It is due to the presence of methyl groups and followed by the cyclization process [43].

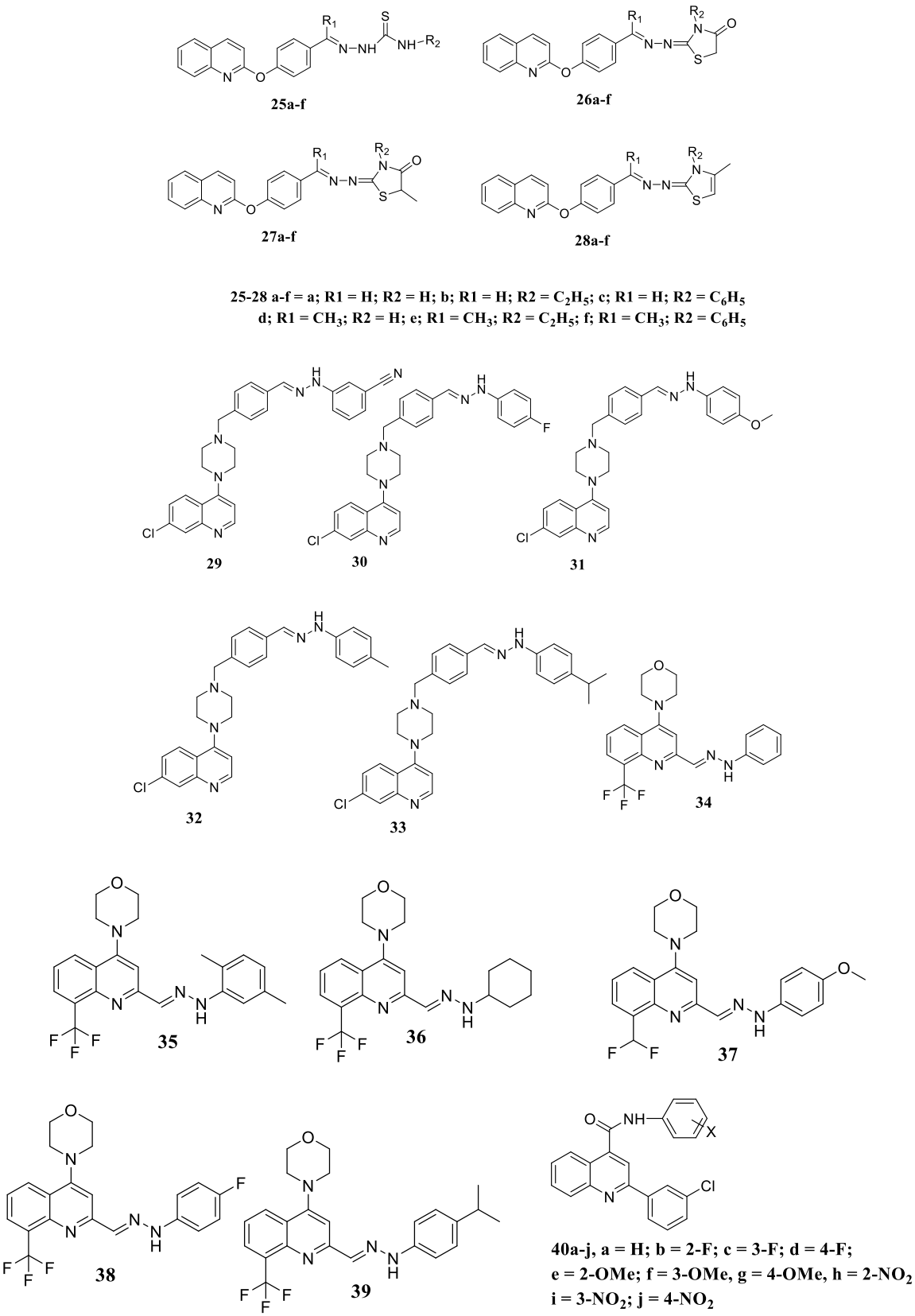



**Figure 5.** Quinoline derivatives used as antibacterial drugs.

Subramanian *et al*. reported a series of novel quinoline-hydrazone derivatives (29-39, Figure 5) and examined their antibacterial activity against various gram-positive and negative bacteria such as *E. coli*, *P. aeruginosa*, *E. faecium*, *S. aureus*, *K. pneumonia*, and *A. baumanii*. Vancomycin and ciprofloxacin were used as references drugs. All the derivatives showed better antibacterial activity against at least two strains. The compounds 32 and 39 exhibit better

antibacterial activity as compared to other compounds against *A. baumanii* with a MIC value of 2 µg/ml [44]. Similarly, Rathod and co-workers reported a series of quinoline derivatives (40 a-j, Figure 5) and exhibited their antibacterial activity against various gram-positive bacteria such as *S. aureus* and *B. subtilis* and gram-negative bacteria such as *E. coli* and *P. aeruginosa*. All most all the synthesized derivatives showed prominent antibacterial activity against all the strains except 40d. The derivative 40h exhibited excellent antibacterial activity against all the strains as compared to other derivatives. The antibacterial activity is moderate to better due to the presence of various functional groups at different positions [45]. The quinoline-based amino acid derivatives (41-44a-e, Figure 6) were used to determine the antibacterial activity against four different bacterial strains such as *E. coli*, *S. aureus*, *B. subtilis*, and *P. aeruginosa*. From the antibacterial activity, it is found that 41a-e and 42a-e showed very weak or negligible antibacterial properties. On the other hand, 43a-e and 44a-e showed moderate to excellent antibacterial activity against all strains. It is due to the presence of carboxylic acid moiety. The authors found that 43a showed excellent antibacterial activity against all the tested strains with a MIC value of 0.62 mg/mL [46].

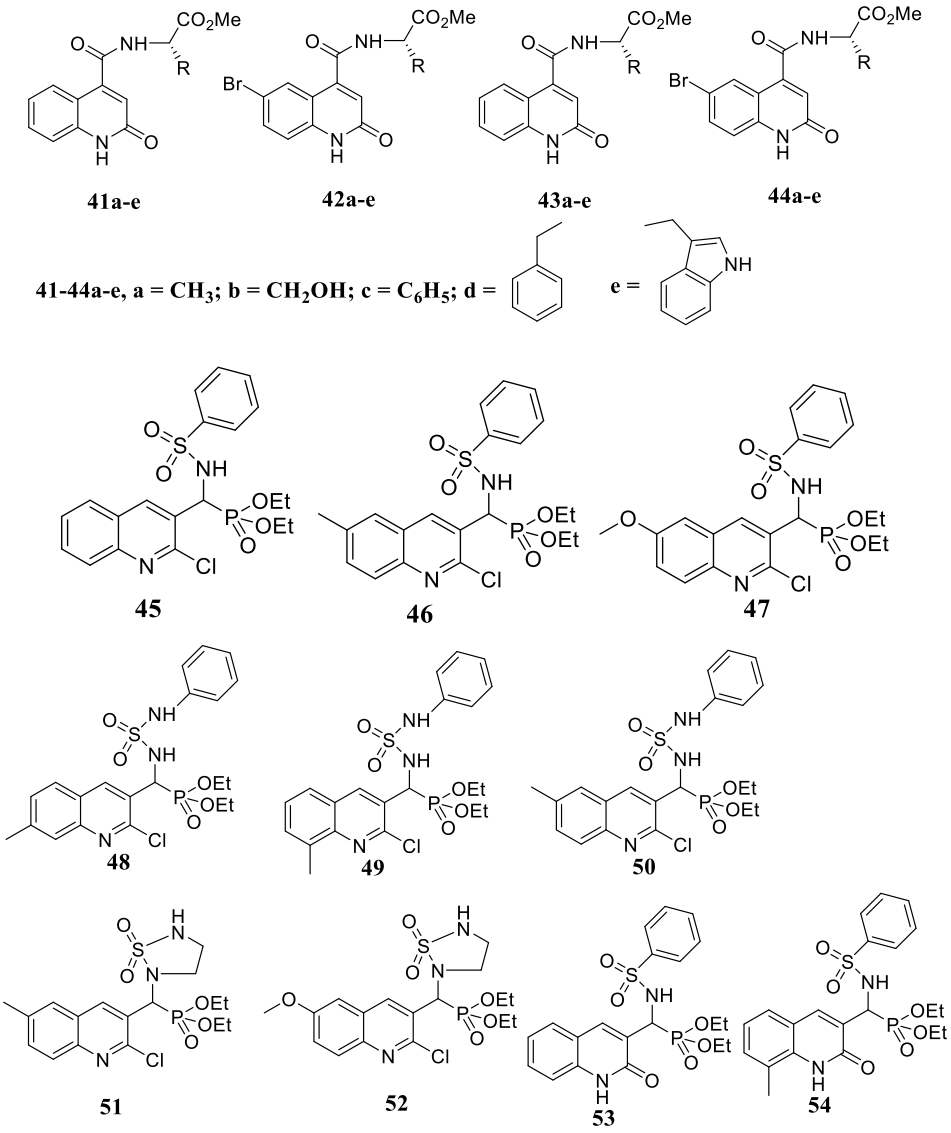
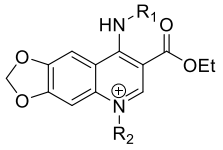



**Figure 6.** Quinoline derivatives used as an antibacterial drugs.

A series of novel sulfonamide-based quinolone and quinolone derivatives (45-54, Figure 6) was designed and synthesized by Bazine *et al*. All the synthesized derivatives

employed for *in vitro* antibacterial activity against various gram-positive and negative strains. All the derivatives exhibited better inhibitory activity (0.125-8 µg/ml) against all strains. Sulfamethoxazole is used as a reference drug [47].



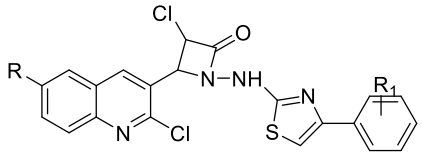
**55-62**

**55, $R_1$ = -$CH_2CH_2Ph$; $R_2$ = -$CH_3$** **56, $R_1$ = -$CH_2CH_2Ph(OCH_3)_2$; $R_2$ = -$CH_3$**

**57, $R_1$ = -$CH_2Ph$; $R_2$ = -$CH_3$** **58, $R_1$ = -$PhOCH_2PH$; $R_2$ = -$CH_3$**

**59, $R_1$ = -$CH_2CH_2Ph$; $R_2$ = -$CH_2CH_2CH_3$** **60, $R_1$ = -$CH_2CH_2Ph(OCH_3)_2$; $R_2$ = -$CH_2CH_2CH_3$**

**61, $R_1$ = -$CH_2Ph$; $R_2$ = -$CH_2CH_2CH_3$** **62, $R_1$ = -$PhOCH_2Ph$; $R_2$ = -$CH_2CH_2CH_3$**



**63a-p**

**R = H and $CH_3$**

**R = -H, -$CH_3$, -4-$OCH_3$, -2-Cl, -4-Cl, -4-Br, -4-F, -4-$NO_2$**

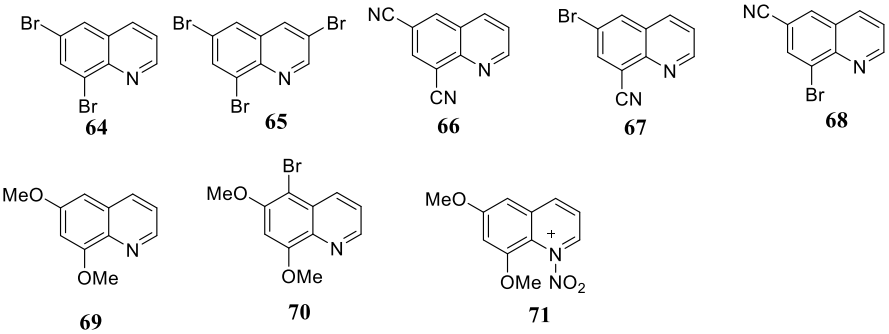
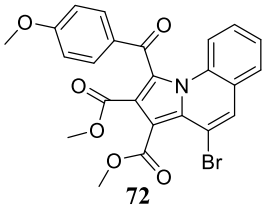


**Figure 7**. Quinoline derivatives used as an antibacterial drugs.

Sun *et al*. reported a series of quinolinium iodide salts derivatives (55-62) and studied their antibacterial activity against *E. coli* and *S. aureus*. All the synthesized derivatives showed better antibacterial activity against the strains compared with the references drug molecule. The authors suggested that the derivatives 58-62 exhibit excellent antibacterial activity against *E. coli* than the references drug such as amoxicillin and ciprofloxacin with MIC values of 6.25-3.125 nmol/mL. On the other hand, these derivatives also envisaged better antibacterial activity against all strains. However, the authors attributed that compound 62 showed excellent antibacterial activity against all tested strains [48]. The antibacterial activity of a series of quinoline scaffolds (63a-p, Figure 7) against various gram-positive and negative bacteria was reported by Khedkar *et al*. From the antibacterial screening. It is observed that all the synthesized derivatives showed moderate to better antibacterial activity against all tested strains.

The derivatives 63b, 63f, 63h, 63i, and 63l showed the highest antibacterial activity against *E. coli* with a MIC value of 100 µg/mL. On the other hand, 63k exhibited excellent antibacterial activity against *P. aeruginosa* with a MIC value of 100 µg/mL. Similarly, 63j and 63k ascribed better antibacterial activity against other tested strains with MIC values of 200

µg/mL. This occurs due to the presence of different functional groups [49]. Taslimi *et al*. designed and synthesized many novel quinoline derivatives (64-71, Figure7) and studied their antibacterial activity against various gram-positive bacteria.

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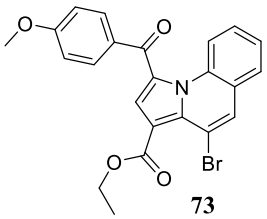


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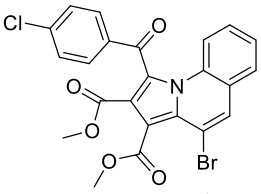


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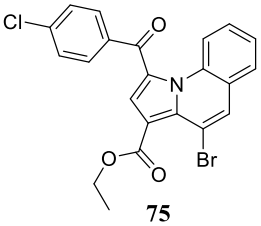


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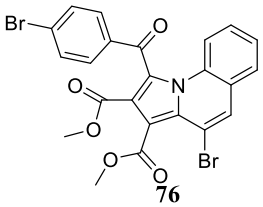


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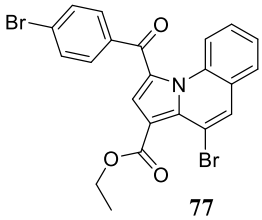


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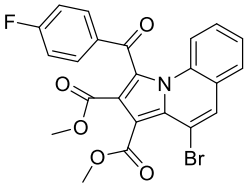


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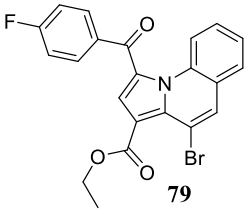


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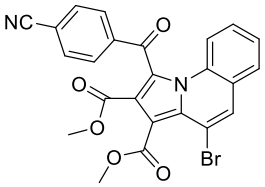


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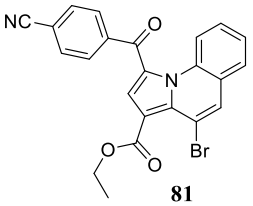


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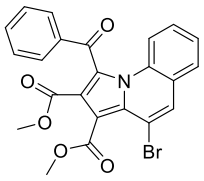


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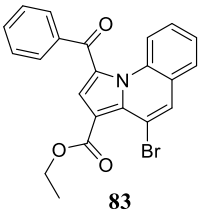


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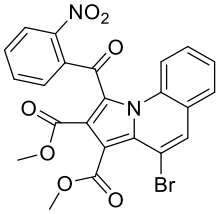


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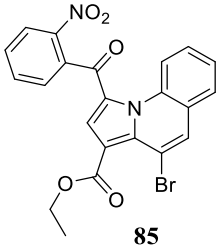


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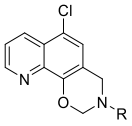
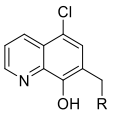
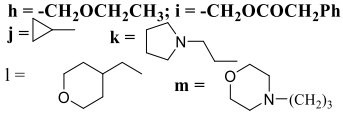


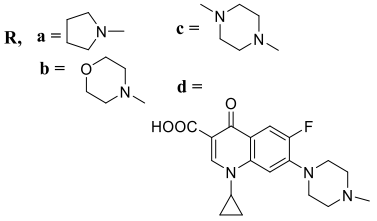

**86a-m**

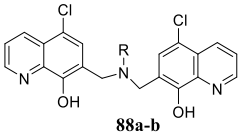



**87a-d**

**R, a = -$CH_3$; b = -$CH_2CH_2CH_3$; c = -$CH(CH_3)_2$**
**d = -$CH_2$-CH=$CH_2$; e = -$CH_2CCH$**
**f = -$CH_2CH_2N(CH_3)_2$; g = -$CH_2CH_2CN$**
**h = -$CH_2OCH_2CH_3$; i = -$CH_2OCOCH_2Ph$**




**88a-b**

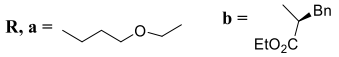


**Figure 8.** Quinoline derivatives used as antibacterial drugs.

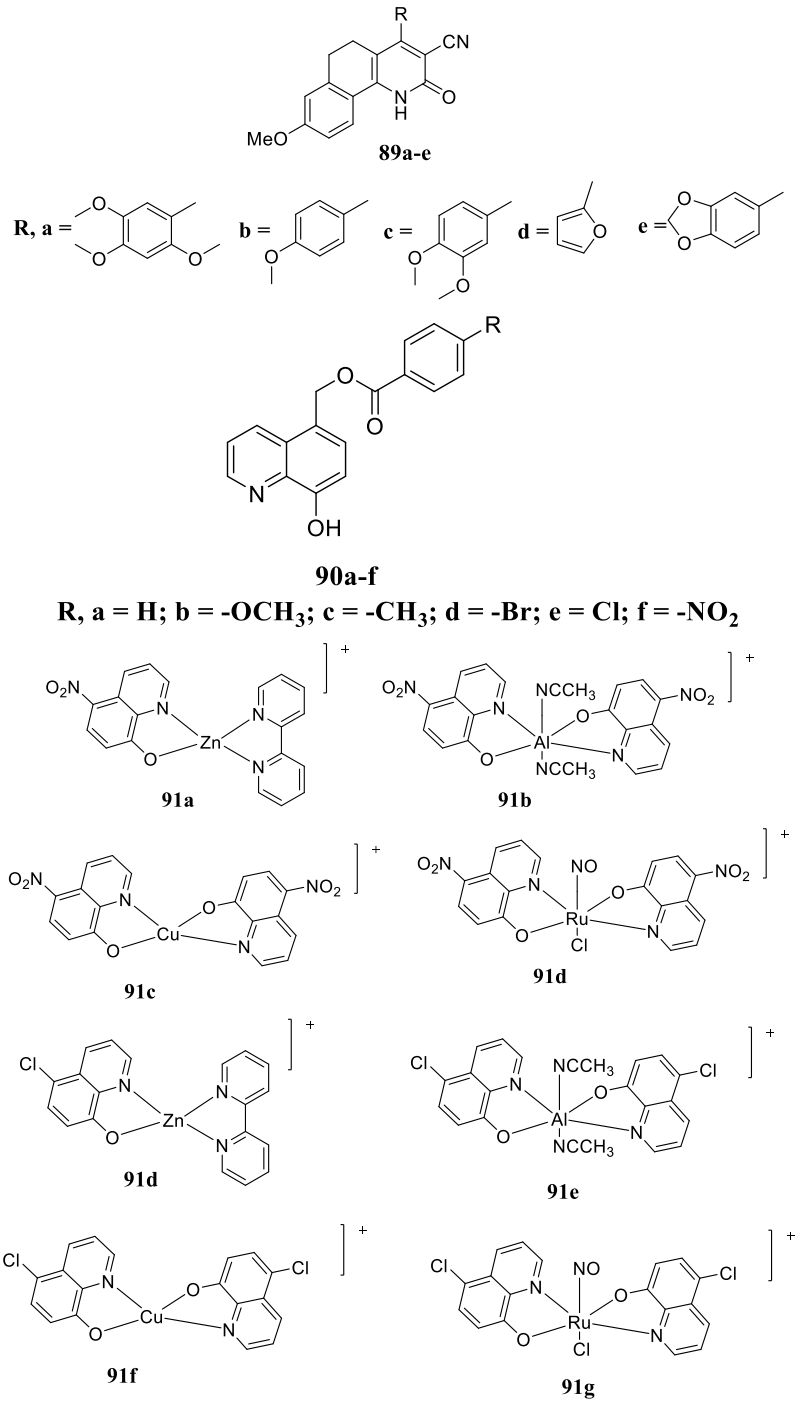
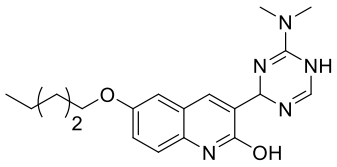



**Figure 9**. Quinoline derivatives used as antibacterial drugs.

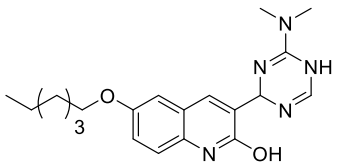
The screening analysis confirms that all the synthesized derivatives showed moderate anti-bacteria activity against all the tested strains. On the other hand, the authors reported that all the synthesized derivatives remain silent towards gram-negative bacteria [50]. Uppar and co-workers developed a series of novel quinoline derivatives (72-85, Figure 8). All the synthesized derivatives were used for antibacterial study against gram-positive bacteria such as *B. subtilis, S. aureus*, and *B. cereus* and gram-negative bacteria such as *E. coli*, *P. aeruginosa*, and *Z. mobilis.* The authors suggested that only 72, 82, and 83 showed prominent antibacterial activity with all tested strains, and the rest of the derivatives remain silent towards the antibacterial properties [51].

Wang *et al*. reported a series of novel quinoline derivatives (86-88, Figure 8) and studied their antibacterial activity against various gram-positive and negative bacteria by the agar diffusion method. The experimental data found that all derivatives show weak antibacterial activity against all tested strains [52]. Novel quinolone-3-carbonitrile derivatives (89a-e, Figure 9) were used to determine the antibacterial activity against various strains by using the disc diffusion method. All the synthesized derivatives show moderate to good antibacterial activity with MIC ranging from 3.13 to 100 μM [53].

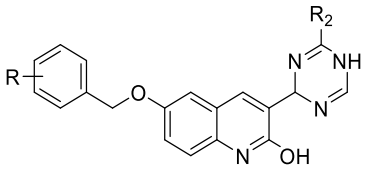
The novel 8-hydroxyquinoline derivatives (90a-f, Figure 9) were designed by Rbaa *et al*. All the synthesized derivatives were used for selective antibacterial activity against various microorganisms using agar disk diffusion assay. The screening analysis showed that 90a ascribes no antibacterial activity against all tested strains. The authors suggested that the presence of electron-donating groups enhanced the antibacterial properties [54]. Bagatin *et al*. reported a series of quinolone derivative metal complexes (M = Zn (II), Cu (II), Al (III) and Ru (II); 91a-h, Figure 9) and examined their antibacterial activity against various gram-positive bacteria such as *E. Faecalis, S. aureus, C. albicans* and gram-negative bacteria such as *E. coli, P. aeruginosa* by using microdilution method. Vancomycin, piperacillin, and fluconazole were used as reference drugs. From the screening analysis, it is observed that 91h exhibited excellent antibacterial activity against all the tested strains with moderate MIC value [55].



**92a**



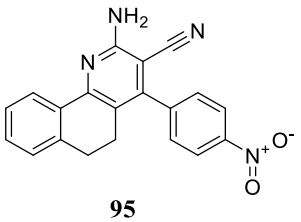
**92b**



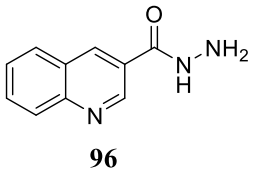
**93a-c**

**94a-m**

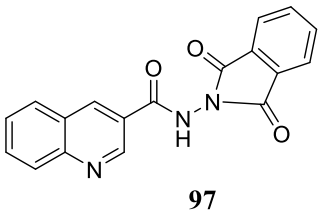
**93a-c, R; a = 3-Cl; b = 2,4-di-Cl; c = 2,6-di-Cl $R_2$ = phenylethanamine**
**94a-m, R; a = 2,4-di-Cl; b = 2,6-di-Cl; c = 2-Cl; d = 3-Cl; e = 4-Cl; f = H**
**g = 2-F; h = 4-F; i = 2-Br; j = 3-$CH_3$; k = 4-$CH_3$, l = 2-CN; m = 4-$NO_2$ $R_2$ = $NHMe_2$**



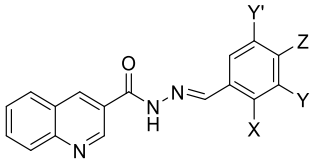
**95**



**96**



**97**



**98a-k**

**98a-k, R = a, X=Y=Z=Y'= H; b, X= OH, Y=Z=Y'= H; c = X= $OCH_3$, Y=Z=Y'= H**
**d, X= Cl, Y=Z=Y'= H; e, X= F, Y=Z=Y'= H; f, X= OH, Y=Y'= Cl, Z =H**
**g = X= OH, Y=Y'= H, Z = OH; h = X= OCH3, Y=Y'= H, Z = OCH3**
**h = X= OCH3, Y=Y'= H, Z = OCH3; i = X= OCH3, Y=Z= H, Y' = OCH3**
**j = Z= F, X=Y=Y'= H; k = Y= F, X=Z=Y'= H**

**Figure 10.** Quinoline derivatives used as an antibacterial drugs.

A series of quinolone-based dihydrotriazine derivatives (92-94, Figure 10) were design and synthesized by Feng *et al*. All the synthesized derivatives were employed for selective detection of anti-bacteria against various strains such as gram-positive bacteria (*S. aureus*) and gram-negative bacteria (*E. coli*). From the antibacterial screening analysis, it is observed that 93a-c showed excellent antibacterial activity against both strains with a MIC value of 2 μg/mL. The authors attributed that the presence of dihydrotriazine moiety enhanced the antibacterial properties [56]. Ceylan *et al*. reported a novel quinolone derivative (95) and examined its antibacterial activity against various gram-positive and negative strains. From the screening analysis, it is found that 95 showed excellent antibacterial activity against all tested strains [57].

Similarly, Sini *et al*. reported a series of novel hydrazine-based quinoline derivatives (96-98). All the synthesized derivatives were used for selective detection of antibacterial activity against two strains such as *E. coli* and *S. aureus*. The screening analysis indicates that all the derivatives showed better antibacterial activity against two tested strains. The derivatives 97, 98g, and 98k ascribed better antibacterial activity than other derivatives. The authors found that all the synthesized derivatives showed better ant-bacterial activity against *E. coli* than *S. aureus* [58].

The foregoing discussions have clearly shown that the quinoline and its derivatives are used as potent antibacterial properties against various strains such as gram-positive and negative bacteria. The skeletal changes have caused the changes in antibacterial properties, and each of the ones computed was selective in showing comparable antibacterial properties.

## 4. Conclusions

Herein, we have described the antibacterial activity of a few quinoline derivatives by cramming the literature available from 2019 and 2020. The quinolines and their derivatives were used as potential drug molecules for antibacterial properties against various strains such as gram-negative and positive bacteria. As a result, quinoline derivatives are used in antibacterial drugs and various potent applications such as catalyst, MOF, dyes-pigments, cosmetic, industrial, and pharmaceuticals. Thus, quinoline derivatives can be considered an auspicious new generation of antibacterial agents and provide scopes to designing molecular imaging experiments that have utility in biological sciences.

In the near future, it is essential to discover new potent molecules for the treatment of multi-resistant gram-negative strains, which are developing at a very rapid rate.

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## Conflicts of Interest

The authors have declared that no competing interests exist.

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