Polycyclic Aromatic Compounds ›
Volume 44, 2024 - Issue 2

Research Articles

Synthesis and Antimicrobial Activity of New Carbohydrazide Bearing Quinoline Scaffolds in Silico ADMET and Molecular Docking Studies

Amol S. Nipate, Chetan K. Jadhav, Asha V. Chate, Prashant P. Dixit, Prachi Sharma & Charansingh H. Gill

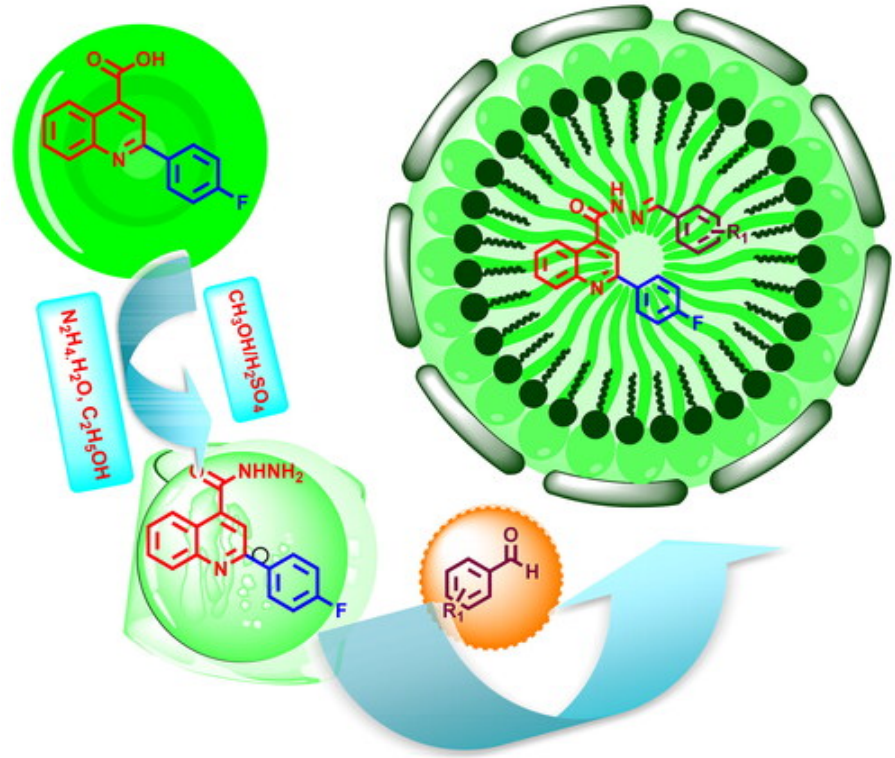
Pages 1348-1365 | Received 14 Sep 2022, Accepted 18 Mar 2023, Published online: 13 Apr 2023

Cite this article https://doi.org/10.1080/10406638.2023.2194653 Check for updates

Abstract

In search of a more potent and new series of fluorine-containing quinoline, hybrid Schiff bases (**6a–o**) analogues were synthesized by a facile and efficient conventional method. They were developed via condensation of quinoline-4-carbohydrazide intermediate and aromatic aldehydes in presence of ethanol. All compounds viz., **6a–o** were efficiently synthesized in good yields in ranges of 76–84%, respectively. All synthesized compounds were well characterized by using various spectroscopic techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR, Mass spectroscopy. Moreover, all newly synthesized hybrid Schiff bases (**6a–o**) have been screened for their antifungal and antibacterial activity. Among these compounds (**6a–d)** shows good antibacterial

niger and compound **6a** was found to inhibit the visible growth of *Staphylococcus aureus* ATCC 6538 at low concentration with MIC 340 µg/.



Display full size

Keywords: Quinoline carbohydrazide quinoline-4-carbohydrazide hybrid Schiff bases antimicrobial activity

1. Introduction

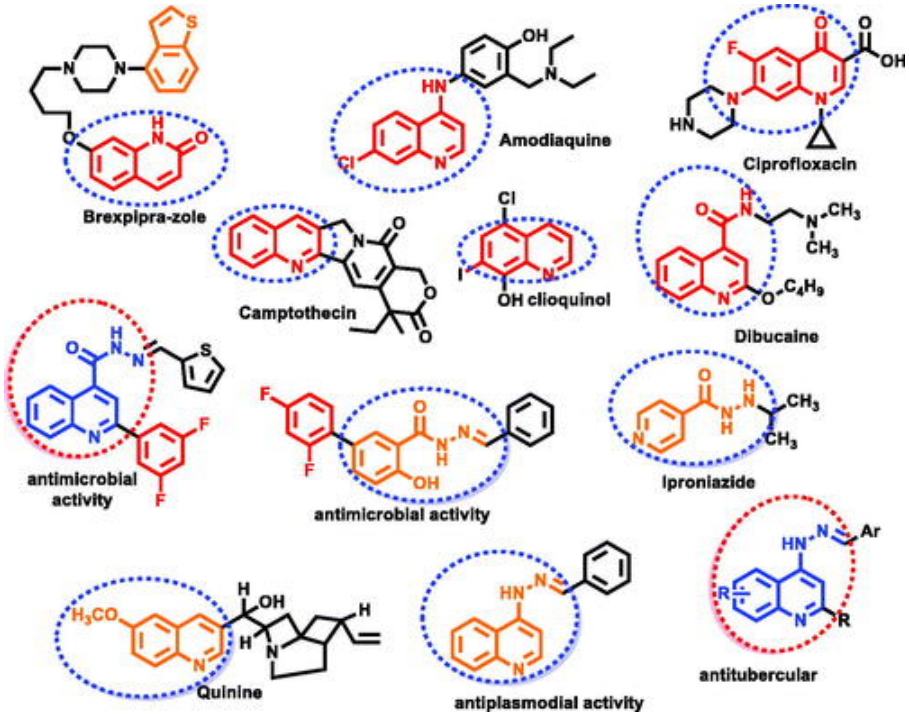
Heterocyclic compounds show great importance in biological and pharmaceuticals processes. In literature we have seen heterocycles as core structures, in many drugs molecule, this has given a spark of interest in designing and synthesizing new heterocyclic compounds.[1–8] The combination of two or more pharmacophores in a single molecule is a well-established hypothesis for the development of more effective drugs.[9–12] Many literature reports have highlighted the enhanced bioactive properties of the combination heterocycles.[13–15] We have a plan to synthesis quinoline and Carbohydrazide (Schiff base) two pharmacophores in a single framework for the development most effective drugs. Quinoline is well known heterocyclic

In this article

inhibitory activity.[16,17] Quinoline scaffold consists of pyridine as a pharmacophore for antimicrobial and anticancer activity including EGFR inhibitory activity.[18] The prominent ones are the antimalarials (Quinine, Mefloquine, Amodiaquinine, Primaquine etc),[19,20] antiviral (Saqinavir), antibacterial (Ciprofloxacin, Spafoxacin, Gatifloxacin, etc),[21,22] antifungal-antiprozoal (Clioquinol), anthelmintic (Oxamniquine),[23,24] a local anesthetic (Dibucaine),[25] antiasthmatic (Montelukast),[26] anticancer (Camptothecin, Irinotecan, Topotecan etc),[27,28] antipsychotic (Aripiprazole, Brexpipra-zole etc),[29] antiglaucoma (Cartiolol),[30] and cardiotonic (Vesnarinone).[31]

Quinoline and its synthetic derivatives have been reported to exhibit various biological activities such as antiviral,[32] anticancer,[33] antibacterial,[34] antifungal,[35] anti-obesity,[36] anti-inflammatory,[37] antimalarial,[38] antituberculosis,[39] hypnotic,[40] antischizophrenic,[41] anti-protozoal,[42] anti-cholesterol,[43] anthelmintic,[44] and analgesic activities,[45] and these activities were demonstrated in drug molecules, which are shown in Figure 1. The scope of the reaction was investigated using different aldehyde contains different functional groups. Structure activity relationship is shown in Figure 2.

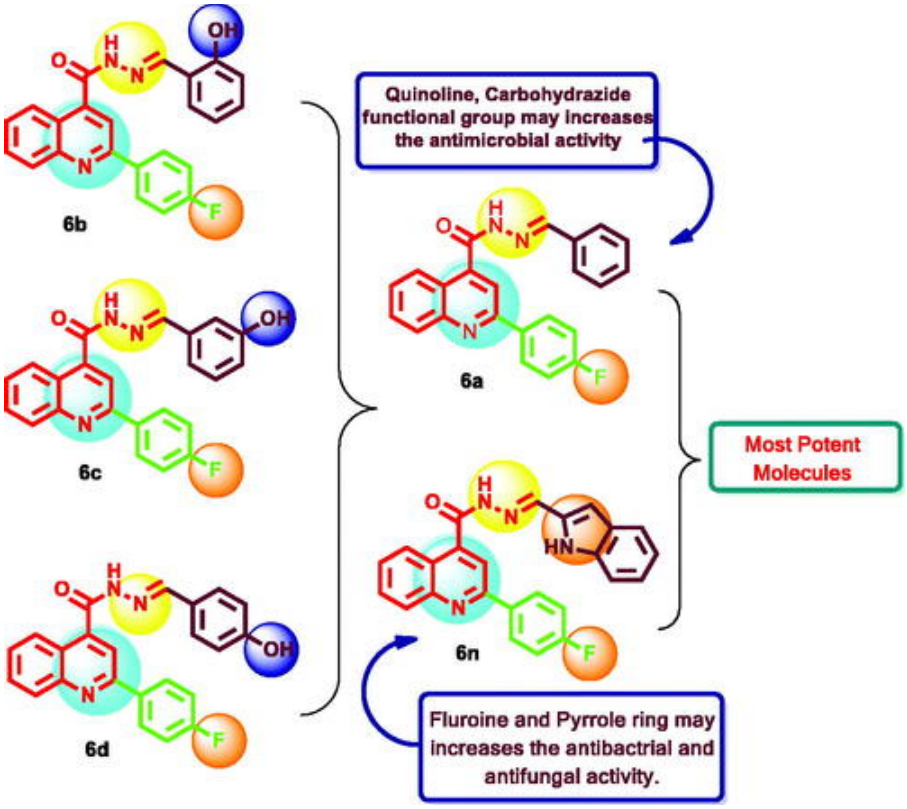
Figure 1. Bioactive heterocycles and drugs containing quinolone as heterocyles.



Display full size

Figure 2. Structure-activity relationship of hybrid compounds.

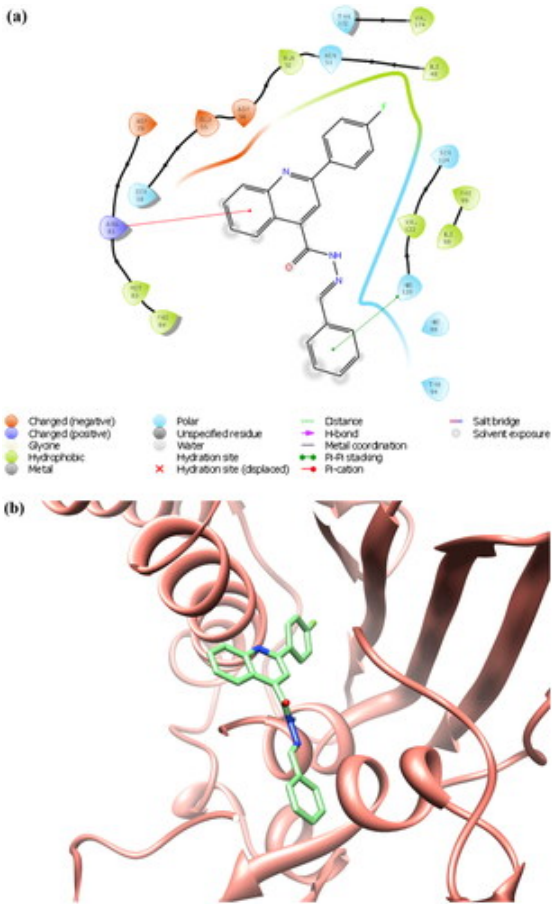
In this article



Display full size

Figure 3. Two-dimensional binding pose of compound **6a** within the *E. coli.* (4MEV) active site.

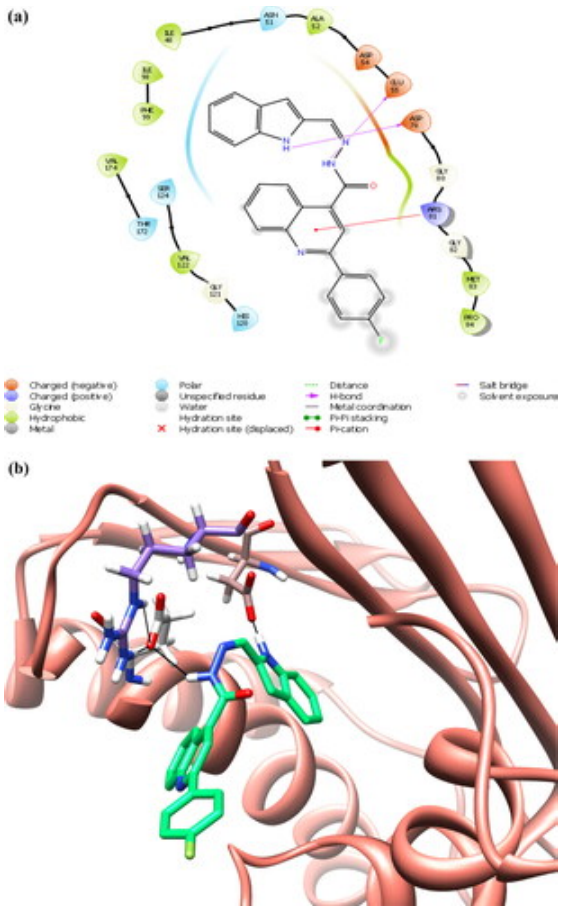
In this article



Display full size

Figure 4. Two-dimensional binding pose of compound **6n** within the *E. coli* (4MEV) active site.

In this article



Display full size

We also report the results of biological screening for possible antibacterial and antifungal activity of the resulting derivatives and we discuss the relationship of molecular structure and the bioactivity Schiff bases, are formed when any primary amine reacts with an aldehyde or a ketone under specific conditions and it's named after the 19th-century first-time preparation of imines was reported by Schiff (1864). We also synthesis the most bioactive compounds belonging to this class, which exhibit antimalarial, antibacterial, antifungal, and/or antiviral activities to have been reported in the literature. Schiff bases and derivatives of this scaffold have been shown to exhibit a large number of biological activities such as antimicrobial, anti-inflammatory, analgesic, anti-tubercular, antibacterial, antioxidant, antiviral, and inhibitors. Therefore, the discovery of new molecules with fluorine groups is very much important in the medicinal chemistry for the potent activity against the diseases, continuing our efforts of the synthesis of biologically active target molecules here, we have reported the synthesis and antifungal and antibacterial activities of some novel substituted **(***E***)**-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide derivatives starting from Isatin and 4-

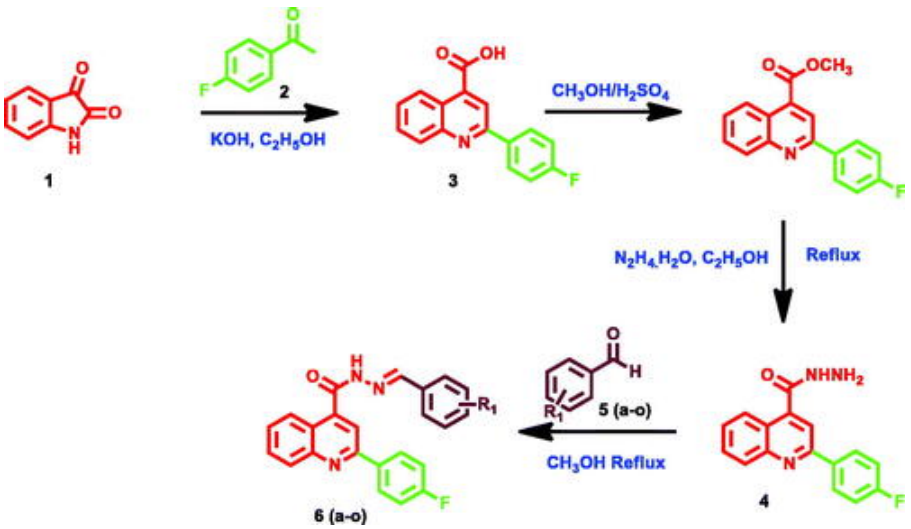
In this article

2. Results and discussion

2.1. Chemistry

The synthetic pathway to achieve the title compounds **(***E*)-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide (**6a–o**) are illustrated in the (Scheme 1**)**. The key intermediate, quinoline-carboxylic acid (**3**) was obtained by commercially available Isatin (**1**). Isatin (**1**) was allowed to react with 4-fluroacetophenone (**2**) in ethanol in presence of potassium hydroxide the resulting mixture was heated under reflux for 4h. The obtained key intermediate quinoline-carboxylic acid (**3**) was treated with hydrazine hydrate followed by esterification in ethanol under refluxed using an oil bath for 10 h to obtain quinoline-4-carbohydrazide (4). In the next step the obtained quinoline-4-carbohydrazide (**4**) was reacted with a different aromatic aldehyde (**5**) in ethanol to give the title compounds **(***E*)-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide (**6a–o**) ie Schiff base, respectively, with better to excellent yield.

Scheme 1. Synthetic protocol for the preparation of **(***E*)-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide.



Display full size

All structures of newly synthesized compounds were analyzed by various spectral technique such as IR, 1H NMR, 13 C, NMR, and mass spectral (MS) analysis. The synthesized compounds were evaluated for their antimicrobial, antibacterial, and antifungal activities. The structural elucidation of the synthesized compounds (**6a–o)** was carried out by FT-IR, ^{1}H NMR, ^{13}C NMR,

In this article

formation of the product as it shows the characteristic absorption peaks at 1671, 1586, and 1314 cm^{-1} which correspond to the C=O, C=N, and C=F stretching, respectively. In ^{1}H NMR spectra of compounds (**6a–o**), a sharp singlet peak of Sec amide proton (NH-) was appeared around s 12.23 ppm and quinolinyl hydrogen for 8.24 (d, 1H), and the disappearance of CHO proton at d 10.15 ppm indicate the formation of quinoline-4-carbohydrazide. ^{13}C NMR spectrum of compound (**6a**). The signal of carbons at 168.4 and 161.7 ppm due to the amide carbonyl and –CF carbon group whereas carbon signal at 130.26 ppm quinoline-2-pyridine carbon, and disappearance of aldehyde carbonyl confirming the formation of a quinoline ring in (**6a**). The HRMS spectrum further strengthen the structure assigned to (**6a**) as **(***E*)-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide showing [M+] ion peak 370.1277 and found 370.1368 for its molecular formula $C_{23}H_{16}FN_3O$. The experimental procedures and spectra of **(***E*)-N'-benzylidene-2-(4-fluorophenyl) quinoline-4-carbohydrazide (**6a–o**) and intermediates are given in supplementary information. The synthetic sequence is represented in

3. Biological screening

3.1. Antimicrobial screening

The in vitro antimicrobial activity of all synthesized compounds was assessed by using the agar well diffusion method by Pramod S. Phatak et al., (2019) with some modifications. For evaluating antibacterial activity Gram-positive and Gram-negative bacterial pathogens were used and for antifungal activity potent fungal pathogens were used. *Staphylococcus aureus* ATCC 6538*, Bacillus cereus* ATCC 14579*, Bacillus megaterium* ATCC 2326, *Micrococcus glutamicum, Bacillus subtilis* ATCC 6633 were Gram-positive pathogens used in this study. *Escherichia coli* ATCC8739*, Salmonella typhi* ATCC9207, *Shigella boydii* ATCC 12034*, Enterobacter aerogenes* ATCC13048*, Pseudomonas aerogenosa* ATCC9027, *Salmonella abony* NCTC6017 were the Gram-negative pathogens used in this study. Antifungal activity of synthesized compounds were determined against *Aspergillus niger* ATCC 16404*, Saccharomyces cereviseae* ATCC 9763, *Candida albicans* ATCC10231 fungal pathogens. Fluconazole and tetracycline were used as antifungal and antibacterial standard reference compounds, respectively. Synthesized compounds were dissolved in DMSO at a concentration of 1 mg/ml. Each bacterium and fungi were inoculated into a sterile Nutrient broth medium and kept at 37 °C for 24 hours for developing inoculums.

diluted to adjust the turbidity to the 0.5 McFarland standards. 200 µL diluted suspension of each pathogen was inoculated on sterile Mueller Hinton agar plates. Wells were punched in the agar medium. Using Micropipette, 100 µl of each compound solution was put in a separate well. 100 µl of DMSO solution without any compound was also placed in a well to check its activity against the pathogenic culture. All Petri dishes were incubated for 24 h at 37 °C . A clear zone around the well was considered a positive result. After complete incubation, the antimicrobial activity of the synthesized compounds was measured. Zones were measured and recorded by using the scale in millimeters (mm). Compound (**6a–d)** showed good antibacterial activity. Compound **6b** was effective against a fungal pathogen *A. niger.* Compound **6 a, c, d,** and **n** showed significant antibacterial activity but didn't show activity against fungal pathogens. Compound **6a** was active against potent Gram-positive and Gram-negative pathogens. Other compounds **6 l** and **6 m** showed effective inhibitory activity against some pathogens.

Minimal inhibitory concentration (MIC)

Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial (compounds) drug that will inhibit the visible growth of a microorganism after overnight incubation. The MIC was determined for **6a** and **6n**. The MIC was determined against *S. aureus* and *E. aerogenes*. The MIC was determined by following the method and guidelines of the Clinical and Laboratory Standard Institute (CLSI). The results are shown in Table 3. The compound **6a** was found to inhibit the visible growth of *S. aureus* ATCC 6538 at low concentration with MIC 340 µg/.

Table 3. MIC values of most potent compounds.

Download CSV Display Table

4. Molecular docking study

Molecular docking studies were performed using Maestro 11.8.[46] For our studies, X-ray crystal structure of transport protein having expression system *E. coli* was taken from PDB entry 4MEV

In this article

were removed. The bond orders and formal charges were added for hetero groups, and hydrogen was added to all atoms in the structure. Side chains that were not close to the binding cavity and do not participate in salt bridges were neutralized. After preparation, the structures were refined to optimize the hydrogen bond network using OPLS_2005 force field. This helps in reorientation of the side chain hydroxyl group. The minimization was terminated when the energy converged or the RMSD reached a maximum cut off of 0.30 A. Grids were then defined around refined structure by entering on ligand using default box size. The extra precision (XP) docking mode for compounds, optimized by Ligprep, was performed on the generated grid of protein structure. The 2-D visualization of the interaction of ligands within the binding site was done in Maestro11.8 only whereas the 3-D visualization of interaction of ligands within the binding site was done using Chimera 1.5.3 which is a freely available tool for visualizing binding poses. Molecular docking analysis was utilized to predict the mechanism of action of the synthesized derivatives for antimicrobial potential.[47–49] All the molecules exhibited binding energies in the range of −33.8 to −57.4 kcal/mol. Tetracycline is showing a large number of interactions within the binding site. The nitrogen of quaternary ammonium part is forming hydrogen bond with GLU 55, carbonyl oxygen of amide which is connected to the ring containing quaternary ammonium part is forming hydrogen bond with ARG 81 whereas oxygen of hydroxyl group present at the fusion of rings is forming hydrogen bond with HIS 120. The hydroxyl group present at the chiral carbon of third ring is forming hydrogen bond with ASN 51 and the oxygen of hydroxyl group present in the terminal benzene ring is forming hydrogen bond with SER 124. In compound **6a** benzene part of quinolone ring show pi-cation interaction with ARG 81 and terminal benzene ring shows pi-pi interaction with HIS 120 (Figure 3). In compound **6n**, the nitrogen of indole ring is forming hydrogen bond with ASP 78 and nitrogen of amide chain is forming hydrogen bond with GLU 55 (Figure 4). The pyridine part of quinolone ring is forming pi-cation interaction with ARG 81. Docking score of the compounds (6a–6o) which are shown in Table 4.

4.1. General

All reagents and solvents were obtained from laboratory-grade and used without further purification. Melting points of all the synthesized compounds were determined in open capillary tubes and are uncorrected (Table 1). Reactions were monitored by thin-layer chromatography (TLC) on silica gel plates (GF 254) using UV light to visualize the course of the reactions. ^{1}H NMR

operating at 400 MHz and 100 MHz spectrometers using DMSO-d_6 TMS as solvent at room temperature. Elemental analyses were obtained on a Thermofischer EA 1112 SERIES CHNS elemental analyzer. Chemical shifts (δ) are reported in ppm with tetramethylsilane (TMS) as an internal standard. Abbreviations for signal couplings are s, singlet; d, doublet; t, triplet; m, multiplet. Mass spectra were recorded on a Sciex, Model; API 107 3000 LCMS/MS Instrument. The purity of each compound was checked by TLC using silica-gel, 60F254 aluminum sheets as 109 adsorbent, and visualization was accomplished by iodine/110 ultraviolet light.

Yield: 93%, M.P.: 250–252 °C ; white solid.

4.1.1. Preparation of 2-(4-fluorophenyl) quinoline-4-carboxylic acid (3)

A compound Isatin (5 g, 0.03398 mol) and solution of potassium hydroxide (10.48 g, 0.1869 mol) in 50 ml water was allowed to stirring for 5 min at room temperature. After the dissolution of all solid a solution of 4-fluroacetophenone (4.6.0 g, 0.03398 mol) in 15 ml of absolute ethanol was added to it stirring, and the reaction mass was heated under reflux for 4 h. After cooling the mixture, the alcohol was removed in a vacuum. The remaining suspension was diluted with 50 ml of water and acidified with glacial acetic acid. The reaction mass was poured on ice-cold water. The white solid obtained was filtered, washed with water, and crystallized from ethanol.

Yield: 98%; M.P. 220–222 °C , brown solid.

FT IR (ATR, n max, cm1): 3270 (broad, OH), 1715 (C=O), 1633(C=N), 1034 (C–F).

^{1}H NMR (400 MHz, DMSO-d_6, δH ppm): 11.06 (s, 1H, CO2H), 7.33 (d, 1H, fluorophenyl-C2H), 7.68–7.71 (m, 1H, quinolinyl-H), 7.40–7.43 (m, 1H, quinolinyl-H), 7.33 (d, 1H, Ar–H, J = 8 Hz), 8.03 (d, 1H, quinolinyl-H, J = 8 Hz), 8.66 (s, 1H, quinolinyl-H), 8.66 (d, 1H, Ar–H).

^{13}C NMR (DMSO-d_6, 100 MHz, d ppm): 116.0, 123.2, 125.1, 127.6, 128.3, 129.0, 130.7, 134.6, 135.6, 147.7, 153.8, 161.5, 167.7.

4.1.2. Preparation of methyl 2-(4-fluorophenyl) quinoline-4-carboxylate (4)

To a solution of 2-(4-fluorophenyl) quinoline-4-carboxylic acid (5 g) in 200 ml of CH_3OH was added 10 ml of conc. H_2SO_4. The resulting reaction mass was refluxed for 15 h, the solvent was removed under reduced pressure, the organic layer was washed with water and brine, dried

purified by recrystallization from ethanol.

Yield: 95% M.P. 82–84 °C white crystalline solid.

^{1}H NMR (400 MHz, DMSO-d_6, d ppm): 3.89 (s, 3H, –OCH3, J = 8 Hz), 6.93 (overlapped dd, 1H, difluorophenyl-C4H), 7.87 (m, 1H, quinolinyl-H), 7.32–7.33 (m, 2H, fluorophenyl-H), 8.10 (d, 1H, quinolinyl-H, J = 8 Hz), 8.66 (dd, 2H, Ar–H), 7.80–7.88 (d, 2H, Ar–H, J = 8 Hz). **^{13}C NMR** (DMSO-d_6, 100 MHz, δ H ppm): 51.5 (OCH_3), 116.3, 122.7, 124.1, 126.4, 126.6, 128.9, 129.6, 136.3, 138.7, 146.3, 155.0, 161.8, (–CF) 165.9 (–CO).

4.1.3. Preparation of 2-(4-fluorophenyl) quinoline-4-carbohydrazide (5)

Methyl 2-(4-fluorophenyl) quinoline-4-carboxylate (0.0120 mol) and hydrazine hydrate (0.060 mol) in 10 ml of ethanol was refluxed using an oil bath for 10 h. The progress of the reaction was monitored by TLC. The excess solvent was then distilled off under reduced pressure and the reaction mass was poured on crushed ice. The product obtained was filtered, washed with water, and crystallized from ethanol.

^{1}H NMR (400 MHz, DMSO-d_6, δH ppm): 9.07 (s, 1H, NH) 4.23 (s, 2H, NH_2), 7.30 (overlapped dd, 2H, fluorophenyl 2H), 7.59–7.68 (m, 1H, quinolinyl-H), 7.33 (m, 1H, Ar–H), 7.94 (d, 1H, Ar–H, J = 8 Hz), 8.03 (s, 1H, Ar–H), 8.24 (d, 1H, quinolinyl-H, J = 8 Hz),

^{13}C NMR (DMSO-d_6, 100 MHz, δH ppm): 106.6, 116.7, 113.9, 120.7, 123.4, 125.7, 129.0, 130.6, 134.2, 135.5, 147.2, 148.8, 153.9, 161.7, 164.4

4.1.4. Preparation of 2-(4-fluorophenyl)-NI-[arylmethylidene]-quinoline-4-carbohydrazides (6a)

To a solution of 2-(4-fluorophenyl) quinoline-4-carbohydrazide (0.0010 mol) in absolute ethanol (10 ml) was added Benzaldehyde (0.0010 mol) and 0.01 ml of glacial acetic acid. The resulting mixture was stirred and refluxed for about 3h. The progress of the reaction was monitored by TLC. After stirring and refluxing for 3h, the mixture was concentrated and the residue was poured on crushed ice. The product obtained was filtered, washed with water, and dried. The crude product was crystallized from ethanol to afford Schiff bases in 80–85% yield.

Yield: 93%, M.P.: 250–252 °C ; white solid.

In this article ^

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 12.23 (s, NH- Sec amide), 8.37–8.45 (d, J = 3.8 Hz, 4H), 7.90–7.75 (Quinoline-2-pyridine 2H), 7.69 (dd, J = 7.0, 1.2 Hz, Ar–H 1H), 7.47 (dd, J = 16.5, 14.8 Hz, Ar–H 4H), 7.26–7.09 (m, Ar–H 1H).

^{13}C NMR (101 MHz, DMSO- $d_{6)}$ δ 168.00 (s amide C=O), 162.05 (s), 161.81 (s), 159.34 (s), 158.84 (s), 154.32 (s Quinoline-2-pyridine), 148.67 (s Quinoline-2-pyridine), 147.44 (s), 144.74 (s), 141.23 (s), 134.20 (d, *J* = 2.9 Hz), 130.00 (Quinoline-2-pyridine s), 129.74 (s), 129.55–128.44 (m), 128.41 (s), 127.91 (s), 127.02 (s), 126.67 (s), 124.65 (d, *J* = 23.2 Hz), 124.27 (s), 123.02 (s), 116.62 (s), 115.72 (d, *J* = 34.9 Hz).

HRMS (ESI)+ calculated for $C_{23}H_{16}FN_3O$ [M+] +: 370.1277 and found 370.1368

Elemental Analysis (%) for $C_{23}H_{16}FN_3O_2$: C, 74.78, H, 4.37, N, 11.38. found C, 74.70, H, 4.30, N, 11.30.

4.1.5. (*E*)-2-(4-fluorophenyl)-N'-(2-hydroxybenzylidene) quinoline-4-carbohydrazide (6b)

Yield: 90%, M.P.: 228–230 °C ; white solid.

^{13}C NMR (101 MHz, DMSO-d_6 ppm) δ 168.76 (s amide C=O), 162.79 (d, J = 26.3 Hz), 157.87 Quinoline-2-pyridine (s), 156.84 (s), 155.15 (s Quinoline-2-pyridine), 149.03 (s), 148.29 (s), 144.66 (s), 143.72 (s), 141.31 (s), 134.98 (s), 132.22 (s), 130.85 (Quinoline-2-pyridine s), 129.48 (s), 129.25 (s), 127.98 (s), 125.45 (d, J = 18.8 Hz), 123.73 (s), 119.91 (s), 117.68 (s), 116.87 (s), 115.15 (s).

Elemental Analysis (%) for $C_{23}H_{16}FN_3O_2$: C, 71.68, H, 4.18, N, 10.90. found C, 71.72, H, 4.20, N, 10.98.

4.1.5. (*E*)-2-(4-fluorophenyl)-N'-(3-hydroxybenzylidene) quinoline-4-carbohydrazide (6c)

Yield: 82%, M.P.: 222–224 °C ; white solid.

Elemental Analysis (%) for $C_{23}H_{16}FN_3O_2$: C, 71.68, H, 4.18, N, 10.90. found C, 71.71, H, 4.16, N, 10.94.

4.1.6. (*E*)-2-(4-fluorophenyl)-N'-(4-hydroxybenzylidene) quinoline-4-carbohydrazide

Yield: 92%, M.P.: 260–262 °C; white solid.

^{13}C NMR (100 MHz, DMSO-d_6 ppm) δ 168.00 (s amide C=O), 162.05 (s), 161.81 (s), 159.34 (s), 158.84 (Quinoline-2-pyridine s), 154.32 (s), 148.67 (s), 147.44 (s), 144.74 (s), 141.23 (s), 130.00 (Quinoline-2-pyridine s), 129.74 (s), 128.41 (s), 127.91 (s), 126.67 (s), 124.65 (d, J = 23.2 Hz), 124.27 (s), 123.02 (s), 116.62 (s), 115.72 (d, J = 34.9 Hz).

Elemental Analysis (%) for $C_{23}H_{16}FN_3O_2$: C, 71.68, H, 4.18, N, 10.90. found C, 71.73, H, 4.21, N, 10.96.

4.1.7. (*E*)-N'-(2-chlorobenzylidene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6e)

Yield: 87%, M.P.: 248–250 °C ; white solid.

Elemental Analysis (%) for $C_{23}H_{15}ClFN_3O$: C, 68.41, H, 3.74, N, 10.41. found C, 68.45, H, 3.78, N, 10.46.

4.1.8. (*E*)-N'-(3-chlorobenzylidene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6f)

Yield: 82%, M.P.: 220–222 °C ; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 8.46–8.39 (m, 2H), 8.37 (d, J = 9.9 Hz, 2H), 8.19 (dd, J = 17.8, 8.3 Hz, 2H), 7.85 (s, Quinoline-2-pyridine 2H), 7.55–7.41 (m, Ar–H 3H), 7.19 (s, Ar–H 2H).

Elemental Analysis (%) for $C_{23}H_{15}ClFN_3O$: C, 68.41, H, 3.74, N, 10.41. found C, 68.40, H, 3.76, N, 10.43.

4.1.9. (*E*)-N'-(4-chlorobenzylidene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6 g)

Yield: 94%, M.P.: 256–258 °C ; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 12.30 (s NH- Sec amide 1H), 8.44 (d, J = 8.7 Hz, 2H), 8.37 (d, J = 3.9 Hz, 2H), 7.90–7.80 (s,Quinoline-2-pyridine 2H), 7.69 (s, 1H), 7.57 (d, J = 8.4 Hz, Ar–H 2H), 7.42 (s Ar–H 2H), 7.19–7.30 (s Ar–H 3H)

In this article ^

(s), 134.35 (s), 132.73 (s), 130.26 (s Quinoline-2-pyridine), 129.42 (d, J = 8.2 Hz), 128.73 (t, J = 10.0 Hz), 124.87 (s), 123.10 (s), 116.92 (s), 115.76 (s).

Elemental Analysis (%) for $C_{23}H_{15}ClFN_3O$: C, 68.41, H, 3.74, N, 10.41. found C, 68.47, H, 3.79, N, 10.48.

4.1.10. (*E*)-N'-(4-fluorobenzylidene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6h)

Yield: 91%, M.P.: 252–254 °C; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 8.47–8.30 (m, Quinoline-2-pyridine 2H), 8.14 (s, 1H), 7.90–7.77 (m, 3H), 7.68 (d, J = 7.3 Hz, Ar–H 1H), 7.57 (s, Ar–H 3H), 7.42 (s, Ar–H 2H), 7.29 (s, Ar–H 2H).

Elemental Analysis (%) for $C_{23}H_{15}F_2N_3O$: C, 71.31, H, 3.90, N, 10.85. found C, 71.37, H, 3.84, N, 10.88.

4.1.11. (*E*)-2-(4-fluorophenyl)-N'-(4-methylbenzylidene) quinoline-4-carbohydrazide (6i)

Yield: 86%, M.P.: 238–240 °C; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 ppm) δ 8.46–8.39 (m, Quinoline-2-pyridine 2H), 8.37 (d, J = 9.9 Hz, 2H), 8.19 (dd, J = 17.8, 8.3 Hz, 2H), 7.85 (s, 2H), 7.78–7.60 (m, Ar–H 2H), 7.55–7.41 (m, Ar–H 3H), 7.19 (s, 1H).

Elemental Analysis (%) for $C_{24}H_{18}FN_3O$: C, 75.18, H, 4.73, N, 10.96. found C, 75.24, H, 4.80, N, 10.92.

4.1.12. (*E*)-2-(4-fluorophenyl)-N'-(2,4,6-trimethoxybenzylidene)quinoline-4-carbohydrazide (6j)

Yield: 88%, M.P.: 276–278 °C ; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 12.22 (s, s NH- Sec amide 1H), 8.44 (d, J = 3.2 Hz, Hz, Quinoline-2-pyridine 2H), 8.30 (s, 1H), 8.22–8.12 (m, 2H), 7.87 (s, 2H), 7.40 (d, J = 6.1 Hz, Ar–H 2H),

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.92 (sec. amide C=O), 154.94 (s), 153.45 (s), 153.05 (s), 148.96 (s), 141.75 (s), 139.70 (s), 130.68 (s Quinoline-2-pyridine), 127.72 (s), 125.30 (s), 123.57 (s), 117.28 (s), 116.19 (s), 104.72 (s), 60.35 (s OCH_3), 56.21 (s OCH_3).

Elemental Analysis (%) for $C_{28}H_{28}FN_3O$: C, 76.61, H, 8.72, N, 7.48. found C, 76.64, H, 8.70, N, 7.44.

4.1.13. (*E*)-2-(4-fluorophenyl)-N'-(4-methoxybenzylidene) quinoline-4-carbohydrazide (6k)

Yield: 80%, M.P.: 236–238 °C .

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 8.48–8.37 (m, Quinoline-2-pyridine 2H), 8.34 (d, J = 17.0 Hz, 6H), 8.21 (s, 2H), 8.15 (s, 2H), 7.90–7.79 (m, Ar–H 3H), 7.74 (d, J = 8.7 Hz, Ar–H 2H), 7.06 (d, J = 8.7 Hz, Ar–H 4H), 3.83 (s, OCH_3 3H).

Elemental Analysis (%) for $C_{24}H_{18}FN_3O_2$: C, 74.28, H, 8.80, N, 7.64. found C, 74.24, H, 8.84, N, 10.60

4.1.14. (*E*)-N'-(4-bromobenzylidene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6 l)

Yield: 85%, M.P.: 270–272 °C ; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 9.67 (s, NH- Sec amide 1H), 8.43 (dd, J = 8.9, 5.5 Hz, Quinoline-2-pyridine 2H), 8.35 (s, 1H), 8.01 − 7.77 (m, 2H), 7.71 − 7.64 (m, 1H), 7.46 − 7.38 (m, 3H), 7.17 − 7.10 (m, Ar–H 2H), 6.88 (d, J = 8.1 Hz, Ar–H 2H).

Elemental Analysis (%) for $C_{23}H_{15}BrFN_3O$: C, 61.62, H, 3.37, N, 9.37. found C, 61.64, H, 3.34, N, 9.34

4.1.15. (*E*)-2-(4-fluorophenyl)-N'-(4-hydroxy-3-methoxybenzylidene)quinoline-4carbohydrazid e (6 m)

Yield: 94%, M.P.: 244–246 °C ; white solid.

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 9.67 (s, NH- Sec amide1H), 8.45 (d, J = 5.6 Hz,

8.3 Hz, 1H), 7.41 (d, J = 15.8 Hz, Ar–H 3H), 7.13 (s, Ar–H 1H), 6.89 (s, Ar–H 1H), 3.87 (s, OCH_3 3H).

Elemental Analysis (%) for $C_{24}H_{18}FN_3O_3$: C, 69.39, H, 4.37, N, 10.12. found C, 69.45, H, 4.42, N, 10.16

4.1.16. (*E*)-N'-((1*H*-indol-2-yl) methylene)-2-(4-fluorophenyl) quinoline-4-carbohydrazide (6n)

Yield: 91%, M.P.: 194–196 °C ; white solid.

Elemental Analysis (%) for $C_{25}H_{17}FN_4O$: C, 73.52, H, 4.20, N, 13.72. found C, 73.45, H, 4.24, N, 13.76

4.1.17. (*E*)-2-(4-fluorophenyl)-N'-(thiophen-2-ylmethylene) quinoline-4-carbohydrazide (6o)

Yield: 85%, M.P.: 242–244 °C ; white solid

^{1}H NMR (400 MHz, DMSO-d_6 δH ppm) δ 12.18 (s, NH- Sec amide1H), 8.41 (Quinoline-2-pyridine 2H), 8.16 (d, J = 8.3 Hz, Ar–H 2H), 7.90–7.84 (m, Ar–H 1H), 7.76–7.62 (m, thiophene2H), 7.53 (d, J = 2.7 Hz, Ar–H 1H), 7.43 (s, 2H), 7.19–7.12 (m, thiophene1H).

Elemental Analysis (%) for $C_{21}H_{14}FN_3OS$: C, 67.18, H, 3.76, N, 11.19. found C, 67.15, H, 3.71, N, 11.14

5. Conclusion

In the summary, a novel series of fluorine-containing quinoline carbohydrazide hybrid Schiff bases (**6a–o**) analogues were developed and screened for their in vitro study in antimicrobial strains by modern medicinal chemistry led to the discovery of a large number of effective drugs. Among all these compounds, **6a–d** showed good antibacterial activity, Compound **6b** was effective against a fungal pathogen *A. niger.* Compound **6a** was active against potent Gram-positive and Gram-negative pathogens. Compound **6 a, c, d,** and **n** showed significant antibacterial activity but didn't show activity against fungal pathogens. Other compounds **6 l** and 6 **m** shows effective inhibitory activity against some pathogens. The compound **6a** was

The MIC was determined for **6a** and **6n**. The MIC was determined against *S. aureus* and *E. aerogenes*. The compound **6a** was found to inhibit the visible growth of *S. aureus* ATCC 6538 at low concentration with MIC 340 µg/. Biological activity and molecular docking study were correlated for the potent molecules.

Author contributions

The manuscript was written through the contributions of all authors. All authors have approved the final version of the manuscript.

Supplemental material

Supplemental Material

Download MS Word (3.6 MB)

Acknowledgments

The author A.S.N is very much thankful to the University Grants Commission of India (UGC), New Delhi, for the award senior research fellowship. The author is also grateful to the Authority of Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431004, India, for providing laboratory facility. We are also thankful to SAIF, CSIR-CDRI, Lucknow, and BITS-Pilani, India, for providing spectral analysis data.

Disclosure statement

No potential conflict of interest was reported by the author(s).

In this article

Table 1. Physical data of synthesized new carbohydrazide derivatives.

Display Table

Table 2. Results of antimicrobial assay of synthesized compounds against potent pathogens.

Download CSV Display Table

Table 4. Docking score of the compounds **6a–6o**.

Download CSV Display Table

References

1. J. Jampilek, "Heterocycles in Medicinal Chemistry," *Molecules* 24, no. 21 (2019): 3839.

PubMed | Web of Science ® | Google Scholar

2. N. Kerru, L. Gummidi, S. Maddila, K. K. Gangu, and S. B. Jonnalagadda, "A Review on Recent Advances in Nitrogen-containing Molecules and Their Biological Applications," *Molecules* 25, no. 8 (2020): 1909.

PubMed | Web of Science ® | Google Scholar

3. M. M. Heravi, and V. Zadsirjan, "Prescribed Drugs Containing Nitrogen Heterocycles: An Overview,"RSC Advances 10, no.72 (2020): 44247–311.

In this article

4. W.-Y. Fang, L. Ravindar, K. P. Rakesh, H. M. Manukumar, C. S. Shantharam, N. S. Alharbi, and H.-L. Qin, "Synthetic Approaches and Pharmaceutical Applications of Chloro-containing Molecules for Drug Discovery: A Critical Review," *European Journal of Medicinal Chemistry* 173 (2019): 117–53.

PubMed | Web of Science ® | Google Scholar

5. P. N. Kalaria, S. C. Karad, and D. K. Raval, "A Review on Diverse Heterocyclic Compounds as the Privileged Scaffolds in Antimalarial Drug Discovery," *European Journal of Medicinal Chemistry* 158 (2018): 917–36.

PubMed | Web of Science ® | Google Scholar

6. C. K. Jadhav, A. S. Nipate, A. V. Chate, V. D. Songire, A. P. Patil, and C. H. Gill, "Efficient Rapid Access to Biginelli for the Multicomponent Synthesis of 1,2,3,4-Tetrahydropyrimidines in Room-temperature Diisopropyl Ethyl Ammonium Acetate," *ACS Omega* 4, no. 27 (2019): 22313–24.

PubMed | Web of Science ® | Google Scholar

7. C. K. Jadhav, A. S. Nipate, A. V. Chate, V. S. Dofe, J. N. Sangshetti, V. M. Khedkar, and C. H. Gill, "Rapid Construction of Substituted Dihydrothiophene Ureidoformamides at Room Temperature Using Diisopropyl Ethyl Ammonium Acetate: A Green Perspective," *ACS Omega* 5, no. 45 (2020): 29055–67.

PubMed | Web of Science ® | Google Scholar

8. A. S. Nipate, C. K. Jadhav, A. V. Chate, T. R. Deshmukh, A. P. Sarkate, and C. H. Gill, "Synthesis and in Vitro Anticancer Activities of New 1,4-Disubstituted-1,2,3-Triazoles Derivatives through Click Approach," *ChemistrySelect* 6, no. 21 (2021): 5173–9.

Web of Science ® | Google Scholar

9. C. Viegas-Junior,, Danuello, A. da Silva Bolzani, V. Barreiro, E. J. Fraga, C. A. M. "Molecular Hybridization: A Useful Tool in the Design of New Drug Prototypes," *Current Medicinal Chemistry* 14, no. 17 (2007): 1829–52. doi:10.2174/092986707781058805

PubMed | Web of Science ® | Google Scholar

In this article

10. A. H. Alkhzem, T. J. Woodman, and I. S. Blagbrough, "Design and Synthesis of Hybrid Compounds as Novel Drugs and Medicines," *RSC Advances* 12, no. 30 (2022): 19470–84.
PubMed | Web of Science ® | Google Scholar

11. C. K. Jadhav, A. S. Nipate, A. V. Chate, A. P. Patil, and C. H. Gill, "Ionic Liquid Catalyzed One-pot Multi-component Synthesis of Fused Pyridine Derivatives: A Strategy for Green and Sustainable Chemistry," *Journal of Heterocyclic Chemistry* 57, no. 12 (2020): 4291–303.
Web of Science ® | Google Scholar

12. A. S. Nipate, C. K. Jadhav, A. V. Chate, K. S. Taur, and C. H. Gill, "β-Cyclodextrin Catalyzed Access to Fused 1,8-Dihydroimidazo[2,3-b]Indoles via One-pot Multicomponent Cascade in Aqueous Ethanol: Supramolecular Approach toward Sustainability," *Journal of Heterocyclic Chemistry* 57, no. 2 (2020): 820–9.
Web of Science ® | Google Scholar

13. T. Shiro, T. Fukaya, and M. Tobe, "The Chemistry and Biological Activity of Heterocycle-fused Quinolinone Derivatives: A Review," *European Journal of Medicinal Chemistry* 97, no. 1 (2015): 397–408.
PubMed | Google Scholar

14. M. C. Mandewale, U. C. Patil, S. V. Shedge, U. R. Dappadwad, and R. S. Yamgar, "A Review on Quinoline Hydrazone Derivatives as a New Class of Potent Antitubercular and Anticancer Agents," *Beni-Suef University Journal of Basic and Applied Sciences* 6, no. 4 (2017): 354–61. doi:10.1016/j.bjbas.2017.07.005
Google Scholar

15. C. K. Jadhav, A. S. Nipate, A. V. Chate, P. M. Kamble, G. A. Kadam, V. S. Dofe, V. M. Khedkar, and C. H. Gill, "Room Temperature Ionic Liquid Promoted Improved and Rapid Synthesis of Highly Functionalized Imidazole and Evaluation of Their Inhibitory Activity against Human Cancer Cells," *Journal of the Chinese Chemical Society* 68, no. 6 (2021): 1067–81. doi:10.1002/jccs.202000468
Web of Science ® | Google Scholar

16. K. George, P. Elavarasan, S. Ponnusamy, and K. Sathananthan, "Facile One-pot Synthesis of Functionalized Quinoline-fused Fluorescent Dihydro/Spiro-quinazolinone Derivatives," *ACS Omega* 7, no. 24 (2022): 20605–18. doi:10.1021/acsomega.2c00674

PubMed | Web of Science ® | Google Scholar

17. C. B. Sangani, J. A. Makawana, Y.-T. Duan, Y. Yin, S. B. Teraiya, N. J. Thumar, and H.-L. Zhu, "Design, Synthesis and Molecular Modeling of Biquinoline–Pyridine Hybrids as a New Class of Potential EGFR and HER-2 Kinase Inhibitors," *Bioorganic & Medicinal Chemistry Letters* 24, no. 18 (2014): 4472–6. doi:10.1016/j.bmcl.2014.07.094

PubMed | Web of Science ® | Google Scholar

18. O. O. Ajani, K. T. Iyaye, and O. T. Ademosun, "Recent Advances in Chemistry and Therapeutic Potential of Functionalized Quinoline Motifs – A Review," *RSC Advances* 12, no. 29 (2022): 18594–614. doi:10.1039/d2ra02896d

PubMed | Web of Science ® | Google Scholar

19. M. Mishra, V. K. Mishra, V. Kashaw, A. K. Iyer, and S. K. Kashaw, "Comprehensive Review on Various Strategies for Antimalarial Drug Discovery," *European Journal of Medicinal Chemistry* 125 (2017): 1300–20. doi:10.1016/j.ejmech.2016.11.025

PubMed | Web of Science ® | Google Scholar

20. E. G. Tse, M. Korsik, and M. H. Todd, "The Past, Present and Future of Anti-malarial Medicines," *Malaria Journal* 18, no. 1 (2019): 93. doi:10.1186/s12936-019-2724-z

PubMed | Google Scholar

21. B. S. Matada, R. Pattanashettar, and N. G. Yernale, "A Comprehensive Review on the Biological Interest of Quinoline and Its Derivatives," *Bioorganic & Medicinal Chemistry* 32 (2021): 115973. doi:10.1016/j.bmc.2020.115973

PubMed | Web of Science ® | Google Scholar

22. M. F. El Shehry, M. M. Ghorab, S. Y. Abbas, E. A. Fayed, S. A. Shedid, and Y. A. Ammar,

(2018): 1463–73. doi:10.1016/j.ejmech.2017.10.046
PubMed | Web of Science ® | Google Scholar

23. S. Kumar, S. Bawa, and H. Gupta, "Biological Activities of Quinoline Derivatives," *Mini Reviews in Medicinal Chemistry* 9, no. 14 (2009): 1648–54. doi:10.2174/138955709791012247
PubMed | Web of Science ® | Google Scholar

24. R. Kaur, and K. Kumar, "Synthetic and Medicinal Perspective of Quinolines as Antiviral Agents," *European Journal of Medicinal Chemistry* 215 (2021): 113220. doi:10.1016/j.ejmech.2021.113220
PubMed | Web of Science ® | Google Scholar

25. Z. Diamant, E. Mantzouranis, and L. Bjermer, "Montelukast in the Treatment of Asthma and Beyond," *Expert Review of Clinical Immunology* 5, no. 6 (2009): 639–58. doi:10.1586/eci.09.62
PubMed | Web of Science ® | Google Scholar

26. B. Furlan, B. T. de Melo, J. Z. B. Papini, M. Sperandio, J. D. Oliveira, E. de Paula, C. M. S. Cereda, and G. R. Tofoli, "Pre-clinical Evaluation of New Dibucaine Formulations for Preventive Analgesia," *Journal of Liposome Research* 31, no. 3 (2021): 230–6. doi:10.1080/08982104.2020.1785494
PubMed | Web of Science ® | Google Scholar

27. D. Sriram, P. Yogeeswari, R. Thirumurugan, and T. Ratan Bal, "Camptothecin and Its Analogues: A Review on Their Chemotherapeutic Potential," *Natural Product Research* 19, no. 4 (2005): 393–412. doi:10.1080/14786410412331299005
PubMed | Web of Science ® | Google Scholar

28. V. J. Venditto, and E. E. Simanek, "Cancer Therapies Utilizing the Camptothecins: A Review of the in Vivo Literature," *Molecular Pharmaceutics* 7, no. 2 (2010): 307–49. doi:10.1021/mp900243b
PubMed | Web of Science ® | Google Scholar

In this article ^

29. J. S. Frankel, and T. L. Schwartz, "Brexpiprazole and Cariprazine: Distinguishing Two New Atypical Antipsychotics from the Original Dopamine Stabilizer Aripiprazole," *Therapeutic Advances in Psychopharmacology* 7, no. 1 (2017): 29–41. doi:10.1177/2045125316672136

PubMed | Web of Science ® | Google Scholar

30. I. A. Subhan, R. Alosaimy, N. T. Alotaibi, B. Mirza, G. Mirza, and O. Bantan, "Evaluation of Compliance Issues to Anti-glaucoma Medications before and after a Structured Interventional Program," *Cureus* 14, no. 6 (2022). doi:10.7759/cureus.25943

Web of Science ® | Google Scholar

31. A. S. Lader, A. Baguisi, R. Casale, S. A. Kates, and R. Beeuwkes, "CMX-2043 Mechanisms of Action In Vitro," *Journal of Cardiovascular Pharmacology* 68, no. 3 (2016): 241–7. doi:10.1097/FJC.0000000000000408

PubMed | Web of Science ® | Google Scholar

32. K. Murugan, C. Panneerselvam, J. Subramaniam, M. Paulpandi, R. Rajaganesh, M. Vasanthakumaran, J. Madhavan, S. Shafi, S. Roni, M. Portilla-Pulido, et al, "Synthesis of New Series of Quinoline Derivatives with Insecticidal Effects on Larval Vectors of Malaria and Dengue Diseases," *Scientific Reports* 12, no. 1 (2022): 4765. doi:10.1038/s41598-022-08397-5

PubMed | Web of Science ® | Google Scholar

33. S. Jain, V. Chandra, P. Kumar Jain, K. Pathak, D. Pathak, and A. Vaidya, "Comprehensive Review on Current Developments of Quinoline-based Anticancer Agents," *Arabian Journal of Chemistry* 12, no. 8 (2019): 4920–46. doi:10.1016/j.arabjc.2016.10.009

Web of Science ® | Google Scholar

34. B. Abdi, M. Fekadu, D. Zeleke, R. Eswaramoorthy, and Y. Melaku, "Synthesis and Evaluation of the Antibacterial and Antioxidant Activities of Some Novel Chloroquinoline Analogs," *Journal of Chemistry* 2021, (2021): 1–13.

Google Scholar

35. G. da Rosa Monte Machado, D. Diedrich, T. C. Ruaro, A. R. Zimmer, M. Lettieri Teixeira, L. F. de

In this article

Derivatives as Promising New Antifungal Candidates for the Treatment of Candidiasis and Dermatophytosis," *Brazilian Journal of Microbiology* 51, no. 4 (2020): 1691–701.
PubMed | Web of Science ® | Google Scholar

36. D. R. Adams, J. M. Bentley, K. R. Benwell, M. J. Bickerdike, C. D. Bodkin, I. A. Cliffe, C. T. Dourish, A. R. George, G. A. Kennett, A. R. Knight, et al, "Pyrrolo(Iso)Quinoline Derivatives as 5-HT(2C) Receptor Agonists," *Bioorganic & Medicinal Chemistry Letters* 16, no. 3 (2006): 677–80.
PubMed | Web of Science ® | Google Scholar

37. S. Mukherjee, and M. Pal, "Medicinal Chemistry of Quinolines as Emerging Anti-inflammatory Agents: An Overview," *Current Medicinal Chemistry* 20, no. 35 (2013): 4386–410.
PubMed | Web of Science ® | Google Scholar

38. M. Foley, and L. Tilley, "Quinoline Antimalarials: Mechanisms of Action and Resistance," *International Journal for Parasitology* 27, no. 2 (1997): 231–40.
PubMed | Web of Science ® | Google Scholar

39. R. S. Keri, and S. A. Patil, "Quinoline: A Promising Antitubercular Target," *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie* 68, no. 8 (2014): 1161–75. doi:10.1016/j.biopha.2014.10.007
PubMed | Web of Science ® | Google Scholar

40. B. Campo, O. Vandal, D. L. Wesche, and J. N. Burrows, "Killing the Hypnozoite – Drug Discovery Approaches to Prevent Relapse in Plasmodium Vivax," *Pathogens and Global Health* 109, no. 3 (2015): 107–22.
PubMed | Web of Science ® | Google Scholar

41. P. Zajdel, K. Marciniec, A. Maślankiewicz, K. Grychowska, G. Satała, B. Duszyńska, T. Lenda, A. Siwek, G. Nowak, A. Partyka, et al, "Antidepressant and Antipsychotic Activity of New Quinoline- and Isoquinoline-sulfonamide Analogs of Aripiprazole Targeting Serotonin 5-HT1A/5-HT2A/5-HT7 and Dopamine D2/D3 Receptors," *European Journal of Medicinal Chemistry* 60 (2013): 42–50.

PubMed | Web of Science ® | Google Scholar

42. A. Dorababu, “Quinoline: A Promising Scaffold in Recent Antiprotozoal Drug Discovery,” *ChemistrySelect* 6, no. 9 (2021): 2164–77.
Web of Science ® | Google Scholar

43. W.-Y. Li, X.-Q. Xiong, D.-M. Zhao, Y.-F. Shi, Z.-H. Yang, C. Yu, P.-W. Fan, M.-S. Cheng, and J.-K. Shen, “Quinoline-3-Carboxamide Derivatives as Potential Cholesteryl Ester Transfer Protein Inhibitors,” *Molecules* 17, no. 5 (2012): 5497–507.
PubMed | Web of Science ® | Google Scholar

44. S. Rossiter, J.-M. Péron, P. J. Whitfield, and K. Jones, “Synthesis and Anthelmintic Properties of Arylquinolines with Activity against Drug-resistant Nematodes,” *Bioorganic & Medicinal Chemistry Letters* 15, no. 21 (2005): 4806–8.
PubMed | Web of Science ® | Google Scholar

45. S. Kumar Gupta, and A. Mishra, “Synthesis, Characterization & Screening for Anti-inflammatory & Analgesic Activity of Quinoline Derivatives Bearing Azetidinones Scaffolds,” *Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry* 15, no. 1 (2016): 31–43.
PubMed | Google Scholar

46. K. J. Bowers, E. Chow, H. Xu, R. O. Dror, M. P. Eastwood, B. A. Gregersen, J. L. Klepeis, I. Kolossvary, M. A. Moraes, F. D. Sacerdoti, J. K. Salmon, Y. Shan, and D. E. Shaw, "Scalable Algorithms for Molecular Dynamics Simulations on Commodity Clusters," Proceedings of the ACM/IEEE Conference on Supercomputing, (2006), 11–17.
Google Scholar

47. H. A. Arjun, G. N. Anil Kumar, R. Elancheran, and S. Kabilan, “Crystal Structure, DFT and Hirshfeld Surface Analysis of (E)-N'-[(1-Chloro-3,4-dihydronaphthalen-2-yl)Methylidene]Benzohydrazide Monohydrate,” *Acta Crystallographica Section E* 76, no. 2 (2020): 132–6.
Google Scholar

In this article

48. H. A. Arjun, R. K. Rajan, R. Elancheran, M. Ramanathan, A. Bhattacharjee, and S. Kabilan, "Crystal Structure, Hirshfeld Surface Analysis, DFT and Molecular Docking Studies on Benzohydrazide Derivatives as Potential Inhibitors of Prostate Cancer," *Chemical Data Collections* 26 (2020): 100350.

Google Scholar

49. H. A. Arjun, R. Elancheran, N. Manikandan, K. Lakshmithendral, M. Ramanathan, A. Bhattacharjee, N. K. Lokanath, and S. Kabilan, "Design, Synthesis, and Biological Evaluation of (E)-N'-((1-Chloro-3,4-Dihydronaphthalen-2-Yl)Methylene)Benzohydrazide Derivatives as Anti-prostate Cancer Agents," *Frontiers in Chemistry* 7 (2019): 474.

Google Scholar