Med Chem Res (2013) 22:635–646
DOI 10.1007/s00044-012-0060-8

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# Synthesis and in vitro antimicrobial and anti-tubercular evaluation of some quinoline-based azitidinone and thiazolidinone analogues

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Received: 18 October 2011 / Accepted: 9 April 2012 / Published online: 22 April 2012


**Abstract** Keeping the objective to build up a new structural class of potent antimicrobials and antituberculosis agents, a series of potentially active quinoline-based azetidinone and thiazolidinone analogues has been synthesized by a simple and efficient synthetic protocol. The thione nucleus formed from 2-chloroquinoline-3-carbaldehyde using sodium sulphide in DMF followed by reaction with various substituted amine to form the corresponding Schiff base intermediates. Attempt has been made to derive final azetidinone and thiazolidinone analogues from Schiff bases by using chloroacetyl chloride and 2-mercapto acetic acid, respectively. Newer analogues were characterized by IR, $^{1}$H NMR, $^{13}$C NMR spectroscopy and elemental analyses. The newly synthesized analogues were then examined for their antimicrobial activity against some bacterial and fungal strains as two Gram −ve bacteria (*Escherichia coli* MTCC 739, *Pseudomonas aeruginosa* MTCC 741), two Gram +ve bacteria (*Staphylococcus aureus* MTCC 96, *Bacillus subtilis* MTCC 430) and two fungal species (*Aspergillus niger* MTCC 282, *Candida albicans* MTCC 183) to develop a novel class of antimicrobial agents and The final compounds were tested for in vitro antituberculosis activity against *Mycobacterium tuberculosis*. *Streptomycin*, Isoniazid, *Rifampicin* and *Ethambutol* were used as standards in this test. These observations provide some predictions to design further antibacterial and antituberculosis active compounds prior to their synthesis according to molecular modeling studies.

**Keywords** 2-Mercapto-quinoline-3-carbaldehyde · Substituted anilines · Azitidinone · Thiazolidinone · Antimicrobial and antituberculosis activity

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## Introduction

Over the past few decades, a rapid increase in the opportunistic microbial infections as well as resistance of microbial pathogens against current chemotherapeutics has been observed. To the human civilization, spreading of such deadly diseases and epidemics is threatening. The rate of mortality is at more serious stage within the patients having decreased immunity and patients under organ transplantation (Vicini *et al*., 2006; McDonald, 2006). Despite the numbers of antimicrobial chemotherapeutics available, the natural occurrence of multidrug resistance in recent years constitutes a substantial need for developing new potentially active antimicrobial entities. A potential approach to overcome the resistance problem is to design innovative agents with a different mode of action so that no cross-resistance with the present therapeuticals can occur. Moreover, the development of drug-resistant strains of mycobacterium species has contributed to the inefficiency of the conventional antituberculosis therapy, thus, it is still necessary to search for new antituberculosis agents. It is well known that the quinoline ring system is an important structural unit widely existing in alkaloids, therapeutics and synthetic analogues with interesting biological activities (Larsen *et al*., 1996; Roma *et al*., 2000; Chen *et al*., 2001). Quinoline is a heterocyclic scaffold of paramount importance to human race. Several quinoline derivatives isolated

from natural resources or prepared synthetically are significant with respect to medicinal chemistry and biomedical use. The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties such as, anti-inflammatory (Eswaran *et al*., 2009), antimicrobial agents (Donnell *et al*., 2010), antituberculosis (Mungra *et al*., 2010), antibacterial (Makawana *et al*., 2011), antitumor activity (Rizvi *et al*., 2011) and antimalarial (Thomas *et al*., 2010). Owing to the mentioned significance, the synthesis of substituted quinolines has been a subject of great interest in organic chemistry. In addition, various fused system of quinolines were studied for their intercalative DNA binding properties. A literature survey reveals that the antitumor activity is due to the intercalation between the base pairs of DNA and interferences with the normal functioning of enzyme topoisomerase II, which is involved in the breaking and releasing of DNA strands (Gatto *et al*., 1999). The antitumor drugs that intercalate DNA are of growing interest in the field of anticancer derivatives. Generally, they are characterized by planar chromophore, which is often constituted by three or four condensed rings, which can intercalate into base pairs. Results of these various binding studies have been useful in designing new and promising anticancer agent for clinical use (Singh *et al*., 1992). An essential component of the search for new leads in the drug designing program is the synthesis of molecules, which are novel yet resemble known biologically active molecules by virtue of the presence of some critical structural features. Certain small heterocyclic molecules act as highly functional scaffolds and are known pharmacophores of a number of biologically active and medicinally useful molecules (Silverman, 1992). There are many methods available for fused quinolines, the Vilsmeier approach has been recently explored by Katritzky and others. More recently, synthesis of functionalized quinoline and their benzo/hetero-fused analogues have been reported from the reaction of α-oxoketene-N,S-acetals with Vilsmeier reagent. It will suffice to mention here that currently available antimicrobial drugs such as *norfloxacin*, *ciprofloxacin* and *ketoconazole* contain quinoline ring in their structures. In fact, 2-chloroquinoline-3-carbaldehyde, the primary intermediate, is a good starting material for the preparation of different quinoline derivatives. In addition, literature survey revealed that quinoline-based azitidinones (Ross *et al*., 2004; Halve *et al*., 2007; Wang *et al*., 2009; Rajasekaran *et al*., 2010; Dua *et al*., 2010; Rokade and Dongare, 2010; Bhat *et al*., 2011) and thiazolidinones (Kumar *et al*., 2007; Bhati and Kumar, 2008; Shingade *et al*., 2011; Desai *et al*., 2011; Pawar and Mulwad, 2004; Patel and Patel, 2010; Pareek *et al*., 2011), the final analogues, are proved as promising antimicrobial agents and antituberculosis agents (Fig. 1).

## Results and discussion

### Chemistry

Various routes have been developed for the synthesis of functionalized quinolines, the Vilsmeier (Meth-Cohn and Bramha, 1978) approach is found to be most efficient. Thus, in this communication the synthesis of 2-chloroquinoline 3-carbaldehyde **2** from *N*-aryl acetamides followed by reaction with Vilsmeier reagent and transformation into different functionalities. The required acetanilide **1** was readily prepared from the reaction of corresponding anilines with acetic anhydride in aqueous medium. The Vilsmeier cyclization of acetanilide **1** was carried out by adding phosphorus oxychloride to the *N*-aryl acetamides in DMF at 0–5 °C followed by heating at 90 °C to afford 2-chloro 3-carbaldehyde **2** in good yield. The IR spectra of compound **2** showed a strong absorption in the range of 1,680–1,696 $cm^{-1}$ for the aldehydic group. The carbaldehyde group in quinolines **2** was also transformed into other functionalities to afford new quinolines which are equally important synthons for the synthesis of fused quinoline systems. Thus, the chloro group in few of the 2-chloro-quinoline 3-carbaldehyde was investigated with various heteronucleophiles. The replacement of chlorine by sulphur, sodium sulphide in DMF was found to be an efficient reagent affording nucleophilic substitution by sulphur and also providing scope for further reaction and one pot cyclisation. The substitution was achieved in an hour at rt to afford thione **3** in quantitative yield. Compound **3** showed prominent peak of thione function group (–SH) at 2,550–2,600 $cm^{-1}$. Thus, carbaldehyde group in quinolines **3** was converted into substituted quinoline Schiff base derivatives **5a–l** in ethanol at refluxed temperature. Schiff base compounds (**5a–l**) showed most prominent peak of imine function group (–C=N–) at 1,645 $cm^{-1}$. The substituted Schiff base derivatives **5a–l** were also reaction with chloroacetylchloride in the presence of triethylamine which act as a catalyst in 1,4 dioxane to undergo cyclization to obtain quinoline azetidin-2-one derivatives **6a–l**. The IR spectrum of compounds **6a–l** which showed sharp peak near 1,736 $cm^{-1}$ indicates the presence of ketone (–C=O) functional group of azetidinone ring. A corresponding peak of C–N–CO was observed at 1,535 $cm^{-1}$. Chlorine functional group exhibited a peak at 770 $cm^{-1}$. The $^{1}H$ NMR spectra of compounds **6a–l** showed the signal at 5.67 parts per million (ppm) due to –CH–Cl on azetidinone ring. Doublets was observed at 6.75 ppm due to CH–N proton on azetidinone ring, singlet was observed at 11.4 ppm due to C–SH proton on quinoline ring, 1.90 ppm due to the presence of $–CH_3$ group at phenyl ring and aromatic protons resonated in the range of 6.85–8.27 ppm. In the $^{1}H$ NMR spectra of the

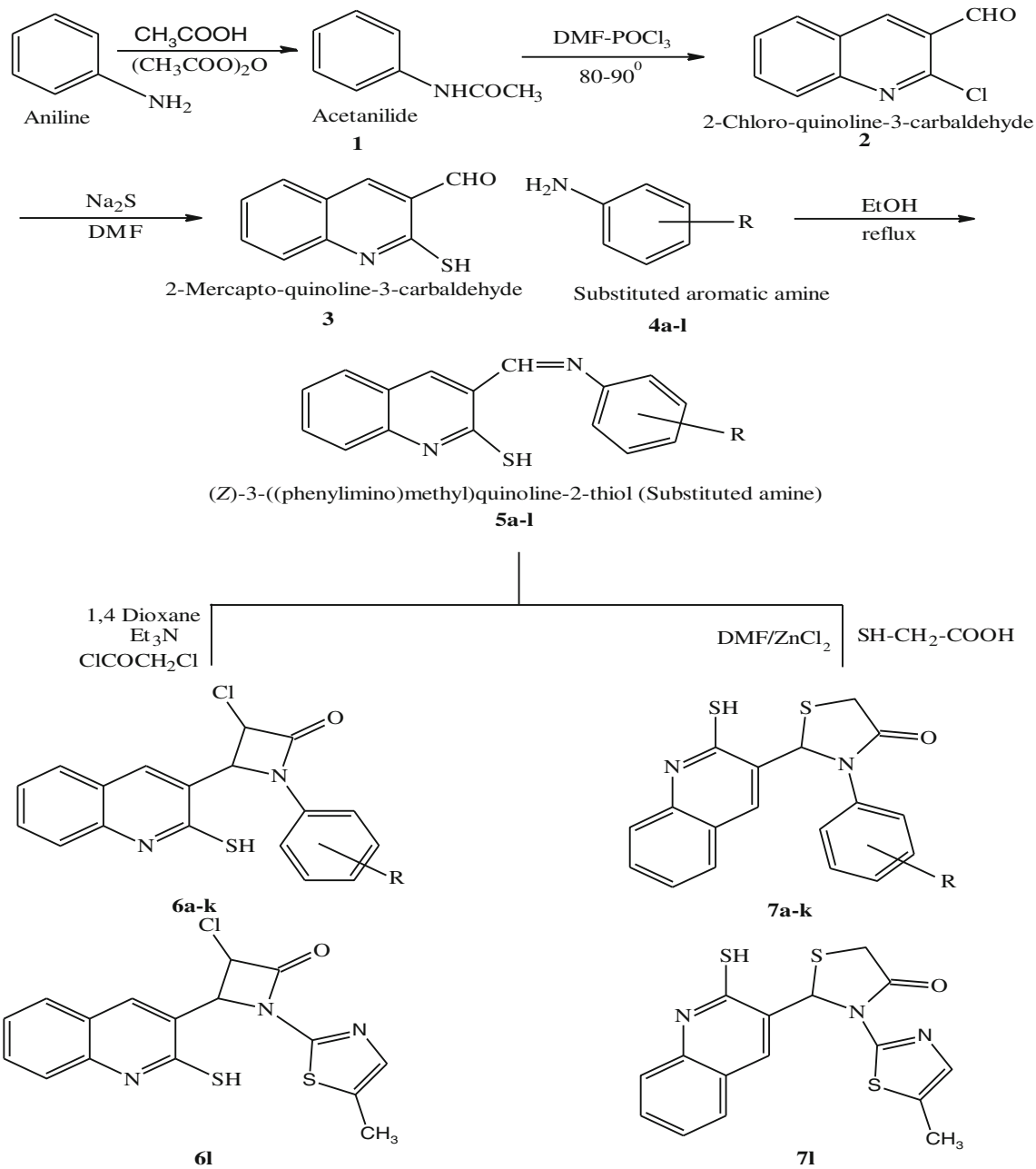


**Fig. 1** Schematic diagram for the synthesis of azitidinone and thiazolidinone derivatives. (*i*) $CH_3COOH$, $(CH_3COO)_2O$; (*ii*) DMF, $POCl_3$, 80–90 °C; (*iii*) $Na_2S$, DMF (*iv*) EtOH, reflux; (*v-a*) 1,4 dioxane, $Et_3N$, $ClCOCH_2Cl$, reflux; (*v-b*) DMF, $ZnCl_2$, $SHCH_2COOH$, reflux

final compounds a peak obtained as doublet in the range 8.14–8.27 ppm was assigned due to the C-3 proton of the quinoline ring, as well as a doublet of doublet was observed at 7.94–8.12 ppm attributed to the C-8 quinoline proton. In addition, C-5, C-2 and C-10 proton atoms of the quinoline ring appeared to resonate at around 7.76–7.87 and 7.51–7.68 ppm. $^{13}C$ NMR spectral assigned signals in the range between 162.21 and 167.58 due to the presence of ketone (–C=O) functional group of azetidinone ring, 60.05–61.76 range showed the presence of (–C–Cl) group of azetidinone ring, 171.14–174.23 ppm range indicates the presence of (–C–SH) group of quinoline ring, 65.86–68.48 range showed the linkage of azetidinone ring, while remaining all aromatic carbons resonated in the range of 120–155.

The same Schiff base derivatives **5a-l** were heated with 2-mercapto acetic acid in the presence of anhydrous zinc chloride which act as a catalyst and solvent DMF undergo cyclisation to give quinoline thiazolidin-4-one derivatives **7a–l**. The IR spectrum of compounds **7a–l** which showed

sharp peak near 1,743 $cm^{-1}$ indicates the presence of ketone (–C=O) functional group of thiazolidinone ring. It also showed corresponding peak of C–N–CO at 1,548 $cm^{-1}$ and showed peak of C–S–C at 637 $cm^{-1}$. The $^1H$ NMR spectra of compounds **7a–l** showed the signal at 6.45 ppm due to –CH–N on thiazolidinone ring. Doublets of doublet was observed at 3.85 ppm due to CH–S proton on thiazolidinone ring, 1.95 ppm due to the presence of $–CH_3$ group at phenyl ring and aromatic protons resonated in the range of 6.98–8.29 ppm. In the $^1H$ NMR spectra of the final compounds a peak obtained as doublet in the range 8.14–8.27 ppm was assigned due to the C-3 proton of the quinoline ring, as well as a doublet of doublet was observed at 7.94–8.12 ppm attributed to the C-8 quinoline proton. In addition, C-5, C-2 and C-10 proton atoms of the quinoline ring appeared to resonate at around 7.76–7.87 and 7.51–7.68 ppm. $^{13}C$ NMR spectral assigned signals in the range between 172.56 and 179.73 due to the presence of ketone (–C=O) functional group of thiazolidinone ring, 55.45–58.68 range showed the linkage of thiazolidinone ring, 161.17–167.53 ppm range indicates the presence of (–C—SH) group of quinoline ring, 34.80–36.59 ppm indicates the presence of $–CH_2$ group in thiazolidinone ring, while remaining all aromatic carbons resonated in the range of 121.53–155.36.

## Antimicrobial activity

The antimicrobial bioassay results summarized in Tables 1 and 2 revealed that some of the newly synthesized azitidinone or thiazolidinone analogues indicated excellent growth inhibitory profiles. It is worth to mention that thiazolidinone analogues displayed better activity against the mentioned microorganisms than that of azitidinone analogues. The minimum inhibitory concentration (MIC) profiles of thiazolidinone analogues were also strong than that of azitidinone class. It was observed that both the class of newly synthesized analogues with electro withdrawing nitro and electro withdrawing halo (–Cl, –F) substituent demonstrated potential antimicrobial properties. Final *azetidinone* compounds **6j**, **6h** and **6k** showed excellent activity against Gram-positive strain *Staphylococcus aureus* at 6.25 μg/mL of MIC. Final *thiazolidinone* compound **7k** showed excellent activity (MIC, 3.12 μg/mL, 25 mm of zone of inhibition) against Gram-positive strain *S. aureus*. Final *azetidinone* analogues **6j**, **6k** and **6l** displayed strong inhibitory action at 6.25 μg/mL, 25 mm of zone of inhibition against Gram-positive *Bacillus subtilis*. Final *thiazolidinone* analogues **7i** and **7j** displayed strong inhibitory action at 3.12 μg/mL, 25 mm of zone of inhibition against Gram-positive *B. subtilis*. Compounds **6g**, **6k** and **6l** was found to contribute promising activity (MIC, 12.5 μg/mL, 25 mm of zone of inhibition) towards Gram-negative strain *Escherichia coli*. Compounds **7f** and **7g** were found to contribute promising activity (MIC, 6.25 μg/mL) towards Gram-negative strain *E. coli*. Compound **6g** appeared with remarkable activity against Gram-negative *Pseudomonas aeruginosa* at 12.5 μg/mL of MIC. Compounds **7i** and **7g** appeared with remarkable activity against Gram-negative *P. aeruginosa* at 12.5 μg/mL of MIC. All the remaining final azitidinone and thiazolidinone derivatives exerted good to moderate activity profile at MIC level ranging from 25 to 100 μg/mL, whereas, some derivatives were found to display weak at a higher concentration of 200–500 μg/mL.

**Table 1** List of coupling compounds **6a–l** and **7a–l**

| | R (substituted –Ar. amines) |
|---|---|
| **a** | Aniline |
| **b** | 2-Methyl aniline |
| **c** | 3-Methyl aniline |
| **d** | 4-Methyl aniline |
| **e** | 2-Nitro aniline |
| **f** | 3-Nitro aniline |
| **g** | 4-Nitro aniline |
| **h** | 2-Chloro aniline |
| **i** | 3-Chloro aniline |
| **j** | 4-Chloro aniline |
| **k** | 4-Floro aniline |
| **l** | 2-Amino 5-methyl thaizole |

The antifungal bioassay results summarized in Table 2 revealed that final *azetidinone* derivatives **6f**, **6g** and **6k** displayed antigrowth activity (MIC, 12.5 μg/mL) against *Aspergillus niger*. The antifungal bioassay results summarized in Table 3 revealed that final *thiazolidinone* derivatives **7k** and **7j** displayed antigrowth activity (MIC, 12.5 μg/mL; 26 mm of zone of inhibition) against *A. niger*. Compound **6k** appeared to inhibit *Candida albicans* at 25 μg/mL. Compound **7k** appeared to inhibit *C. albicans* at 12.5 μg/mL. Compound 7**j** indicated half fold activity (25 μg/mL) than the most active analogues tested towards *C. albicans*. All the remaining final *azitidinone* and *thiazolidinone* derivatives were found to demonstrate good to moderate activity profile at MIC level ranging from 25 to 100 μg/mL, whereas, some final derivatives were found to display weak activity at a higher concentration of 200–500 μg/mL (Table 4).

## Antituberculosis activity

In vitro tuberculosis activities of compounds **6a–l** and **7a–l** were assessed against *Mycobacterium tuberculosis* H37Rv. The results indicated that both *azetidinone* and *thiazolidinone* analogues were active against mycobacteria.

**Table 2** In vitro antimicrobial study (MIC μg/mL) of *azetidinone* analogues **6a–l** MIC

| Compd no. (100 μg/disc) | R | Gram negative | | Gram positive | | Fungal species | |
|---|---|---|---|---|---|---|---|
| | | *S. aureus* | *B. subtilis* | *E. coli* | *P. aeruginosa* | *A. niger* | *C. albicans* |
| **6a** | Aniline | 17 (100) | 17 (100) | <10 (100) | <10 (100) | <10 (100) | <10 (100) |
| **6b** | 2-Methyl aniline | 21 (62.5) | <10 (100) | <10 (100) | 19 (100) | 18 (100) | 20 (100) |
| **6c** | 3-Methyl aniline | 19 (100) | 18 (100) | 17 (100) | <10 (100) | 19 (100) | 18 (100) |
| **6d** | 4-Methyl aniline | 18 (100) | 19 (100) | 18 (100) | 18 (100) | 17 (100) | 15 (100) |
| **6e** | 2-Nitro aniline | 22 (62.5) | 22 (62.5) | 21 (62.5) | 24 (25) | 23 (25) | 21 (62.5) |
| **6f** | 3-Nitro aniline | 22 (50) | 22 (50) | 22 (50) | 23 (50) | 24 (12.5) | 20 (100) |
| **6g** | 4-Nitro aniline | 24 (50) | 24 (25) | **25 (12.5)** | **24 (12.5)** | 24 (12.5) | 20 (100) |
| **6h** | 2-Chloro aniline | 24 (6.25) | 25 (12.5) | 23 (50) | 22 (50) | 20 (62.5) | 19 (100) |
| **6i** | 3-Chloro aniline | 24 (12.5) | 25 (12.5) | 22 (62.5) | 23 (62.5) | 25 (50) | 21 (62.5) |
| **6j** | 4-Chloro aniline | **26 (6.25)** | **25 (6.25)** | 24 (25) | 24 (25) | 25 (25) | 22 (100) |
| **6k** | 4-Floro aniline | **26 (6.25)** | **25 (6.25)** | 24 (12.5) | 23 (25) | **25 (12.5)** | **24 (25)** |
| **6l** | 2-Amino 5-methyl thaizole | 24 (25) | 22 (6.25) | 24 (12.5) | 22 (100) | 22 (50) | 24 (62.5) |
| Ciprofloxacin (100 μg/disc) | | 30 (≤1) | 31 (≤1) | 32 (≤1) | 33 (≤1) | – | – |
| Ketoconazole (100 μg/disc) | | – | – | – | – | 30 (≤3) | 33 (≤1) |
| DMSO | | – | – | – | – | – | – |

The MIC values were evaluated at concentration range of 3.12–100 μg/mL

Data values in bold letter represents the highest activity

**Table 3** In vitro antimicrobial study (MIC μg/mL) of *thiazolidinone* analogues **7a–l** MIC

| Compd no. (100 μg/disc) | R | Gram negative | | Gram positive | | Fungal species | |
|---|---|---|---|---|---|---|---|
| | | *S. aureus* | *B. subtilis* | *E. coli* | *P. aeruginosa* | *A. niger* | *C. albicans* |
| **7a** | Aniline | 19 (100) | 17 (100) | 16 (100) | 17 (100) | 16 (100) | 15 (100) |
| **7b** | 2-Methyl aniline | 20 (100) | 15 (100) | 15 (100) | 14 (1,000) | 16 (100) | 17 (100) |
| **7c** | 3-Methyl aniline | 21 (62.5) | 19 (100) | 19 (100) | 18 (100) | 20 (100) | 19 (100) |
| **7d** | 4-Methyl aniline | 20 (100) | 20 (100) | 19 (100) | 19 (100) | 17 (100) | 15 (100) |
| **7e** | 2-Nitro aniline | 22 (62.5) | 23 (62.5) | 23 (62.5) | 23 (25) | 23 (50) | 22 (100) |
| **7f** | 3-Nitro aniline | 22 (50) | 22 (50) | **24 (6.25)** | 23 (25) | 23 (25) | 20 (100) |
| **7g** | 4-Nitro aniline | 23 (12.5) | 23 (50) | 23 (6.25) | 24 (12.5) | 25 (25) | 18 (100) |
| **7h** | 2-Chloro aniline | 23 (6.25) | 25 (12.5) | 23 (12.5) | 23 (62.5) | 21 (62.5) | 22 (62.5) |
| **7i** | 3-Chloro aniline | 24 (6.25) | **25 (3.12)** | 22 (50) | **25 (12.5)** | 25 (50) | 22 (50) |
| **7j** | 4-Chloro aniline | 25 (6.25) | **25 (3.12)** | 23 (25) | 24 (25) | 25 (12.5) | 24 (25) |
| **7k** | 4-Floro aniline | **25 (3.12)** | 25 (6.25) | 24 (12.5) | 24 (50) | **26 (12.5)** | **26 (12.5)** |
| **7l** | 2-Amino 5-methyl thaizole | 24 (12.5) | 23 (25) | 24 (12.5) | 23 (62.5) | 23 (62.5) | 24 (62.5) |
| Ciprofloxacin (100 μg/disc) | | 30 (≤1) | 31 (≤1) | 32 (≤1) | 33 (≤1) | – | – |
| Ketoconazole (100 μg/disc) | | – | – | – | – | 30 (≤3) | 33 (≤1) |
| DMSO | | – | – | – | – | – | – |

The MIC values were evaluated at concentration range of 3.12–100 μg/mL

Data values in bold letter represents the highest activity

Preliminary antituberculosis screening results using BACTEC MGIT method revealed that final *azetidinone* analogues **6j** and **6k** as well as *thiazolidinone* analogues **7g**, **7j**, **7k** and **7l** analogues displayed highest inhibition at a constant concentration level (62.5 μg/mL) against *M. tuberculosis* H37Rv.

## Experimental

### Materials and methods

All the chemicals used in the synthesis were of analytical grade. The melting points were determined in open capillary

**Table 4** Antituberculosis activity of *azetidinone* and *thiazolidinone* analogues

| Compounds | R | MIC (μg/mL) *M. Tuberculosis* (H37Rv) |
|---|---|---|
| **6a** | Aniline | 1,000 |
| **6b** | 2-Methyl aniline | 500 |
| **6c** | 3-Methyl aniline | 500 |
| **6d** | 4-Methyl aniline | 250 |
| **6e** | 2-Nitro aniline | 500 |
| **6f** | 3-Nitro aniline | 250 |
| **6g** | 4-Nitro aniline | 250 |
| **6h** | 2-Chloro aniline | 125 |
| **6i** | 3-Chloro aniline | 125 |
| **6j** | 4-Chloro aniline | **62.5** |
| **6k** | 4-Floro aniline | **62.5** |
| **6l** | 2-Amino 5-methyl thaizole | 125 |
| **7a** | Aniline | 1,000 |
| **7b** | 2-Methyl aniline | 500 |
| **7c** | 3-Methyl aniline | 500 |
| **7d** | 4-Methyl aniline | 250 |
| **7e** | 2-Nitro aniline | 250 |
| **7f** | 3-Nitro aniline | 125 |
| **7g** | 4-Nitro aniline | **62.5** |
| **7h** | 2-Chloro aniline | 125 |
| **7i** | 3-Chloro aniline | 125 |
| **7j** | 4-Chloro aniline | **62.5** |
| **7k** | 4-Floro aniline | **62.5** |
| **7l** | 2-Amino 5-methyl thaizole | **62.5** |
| Rifampicin | | 40 |
| Isoniazid | | 0.2 |

Data values in bold letter represents the highest activity

on Veego electronic apparatus VMP-D (Veego Instrument Corporation, Mumbai, India) and are uncorrected. The IR spectra (4,000–400 $cm^{-1}$) of synthesized compounds were recorded on Shimadzu 8400-S FT-IR spectrophotometer (Shimadzu India Pvt. Ltd., Mumbai, India) using KBr pellets. Thin layer chromatography was performed on microscopic glass slides (2 × 7.5 cm) coated with silica gel-G, using appropriate mobile phase system and spots were visualized under UV radiation. $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on a Varian 400 MHz model spectrometer (Varian India Pvt. Ltd., Mumbai, India) using DMSO as a solvent and TMS as internal standard with $^{1}H$ resonant frequency of 400 MHz and $^{13}C$ resonant frequency of 400 MHz. The $^{1}H$ NMR and $^{13}C$ NMR chemical shifts were reported as ppm downfield from TMS ($Me_4Si$) and $CFCl_3$ and were performed at centre for excellence, Vapi, India. The splitting patterns are designated as follows: s—singlet, d—doublet and m—multiplet. Elemental analyses (C, H, N) were performed using a Heraeus Carlo Erba 1180 CHN analyzer (Hanau, Germany).

## Methods of in vitro evaluation of antimicrobial and antitubercular activity

Synthesized *quinoline* derivatives **6a–l** and **7a–l** were examined for antimicrobial activity against several bacteria (*Staphylococcus aureus* MTCC 96, *Bacillus subtilis* MTCC 430, *Escherichia coli* MTCC 739, *Pseudomonas aeruginosa* MTCC 741) and fungi (*Aspergillus niger* MTCC 282, *Candida albicans* MTCC 183) using agar streak dilution method (Hawkey and Lewis, 1994) as well as against *M. tuberculosis* H37Rv strain using BACTEC MGIT method (Anargyros *et al*., 1990). Ciprofloxacin and ketoconazole (100 μg/disc) were used as control drugs for antibacterial and antifungal activity, respectively, and assayed for MICs at the concentration levels 1000, 500, 250, 125 and 62.5 μg/mL in this study.

## General procedure for the synthesis of 2-chloroquinoline 3-carbaldehyde (**2**)

To a solution of **1** (15 g, 0.05 mol) in dry DMF (24.5 mL, 0.15 mol) at 0–5 °C with stirring $POCl_3$ (204.1 mL, 0.6 mol) was added dropwise and the mixture was stirred at 80–90 °C for time ranging between 4 and 15 h. The mixture was poured into crushed ice, stirred for 5 min and the resultant was solid filtered, washed well with water and dried. The compounds were purified by recrystallisation from either ethyl acetate or acetonitrile. Yield: 85 %, m.p. 146–149 °C (dec.). IR (KBr) $cm^{-1}$: 1,680–1,696 $cm^{-1}$ (–CHO).

## Synthesis of 2-mercapto-quinoline-3-carbaldehyde (**3**)

To a solution of **2** (0.01 mol) in dry DMF (50 mL), sodium sulphide (0.015 mol) was added and stirred for 1–2 h at rt. On completion of the reaction (monitored by TLC), the reaction mixture was poured into crushed ice and made acidic with acetic acid. The product was filtered off, washed well with water, dried to give desired compounds **3**. The compounds were purified by recrystallisation from DMF. Yield 83 %, m.p. 283–285 °C (dec.). IR (KBr) $cm^{-1}$: 1,687–1,693 $cm^{-1}$ (–CHO), 2,575–2,595 $cm^{-1}$ (–SH) (Raghavendra *et al*., 2008; Halehatty *et al*., 2009).

## General procedure for the Synthesis of (*Z*)-3-((phenylimino)methyl)quinoline-2-thiol (substituted amine) **5a–l**

2-Mercapto-quinoline-3-carbaldehyde (0.01 mol) **3**, substituted aromatic amine **4a–l** (0.01 mol) were taken in

ethanol with catalytic amount of conc. $H_2SO_4$ (2 mL) and heated to refluxed for 6–7 h. After conclusion of the reaction (TLC), the reaction mixture was poured onto crushed ice; the solid mass thus separated out was filtered, washed with water and dried to give desired compounds **5a–l**. The compounds were purified by recrystallisation from ethanol.

General procedure for preparation of compounds **6a–l**

A mixture of (*Z*)-3-((phenylimino)methyl)quinoline-2-thiol (substituted amine) **5a–l** (0.01 mol) and triethylamine (0.02 mol) was dissolved in 1,4-dioxane (50 mL). To this well-stirred cooled solution chloroacetylchloride (0.02 mol) was added dropwise during 30 min. The reaction mixture was then stirred for further 1 h and refluxing for 10 h. the triethylamine hydrochloride salt formed was filtered to separate the salt. The filtrate was concentrated to half of its initial volume and then poured onto crushed ice. The product obtained was filtered, washed with water and recrystallized from ethanol.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-phenylazetidin-2-one (**6a**)*

Yield: 79 %. m.p. 220–223 °C (DMF). IR (KBr) $cm^{-1}$: 2585 (S–H), 1731 (C=O), 1589 (C=C), 1531 (C–N), 760 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.4 (s, 1H, –SH), 8.17 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 8.05 (dd, $J = 7.9$, 1.6 Hz, 1H, H8, quinoline), 7.78 (dd, $J = 7.3$, 1.9 Hz, 1H, H5, quinoline), 7.63–7.52 (m, 2H, quinoline), 7.42–7.20 (m, 5H, Ar–H), 6.51 (d, $J = 6.7$ Hz, 1H, CH–N at azitidinone ring), 5.88 (d, $J = 6.7$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.15 (1C, C-8, C–SH), 163.97 (1C, C-20, C=O), 154.15–119.20 (14C, Ar–C), 67.95 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.19 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{13}ClN_2OS$: C, 63.43; H, 3.84; N, 8.22. Found: C, 63.55; H, 3.93; N, 8.34.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-o-tolylazetidin-2-one (**6b**)*

Yield: 73 %. m.p. 245–248 °C (DMF). IR (KBr) $cm^{-1}$: 2581 (S–H), 1738 (C=O), 1585 (C=C), 1537 (C–N), 770 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.7 (s, 1H, –SH), 8.20 (d, $J = 1.6$ Hz, 1H, H3, quinoline), 8.11 (dd, $J = 7.7$, 1.4 Hz, 1H, H8, quinoline), 7.80 (dd, $J = 7.5$, 1.7 Hz, 1H, H5, quinoline), 7.65–7.53 (m, 2H, quinoline), 7.44–7.19 (m, 4H, Ar–H), 6.57 (d, $J = 6.6$ Hz, 1H, CH–N at azitidinone ring), 5.90 (d, $J = 6.5$ Hz, 1H), 1.90 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 171.18 (1C, C-8, C–SH), 165.67 (1C, C-20, C=O), 155.24–118.31 (14C, Ar–C), 66.68 (1C, C-12, –Ar.–Azetidinone ring linkage), 61.23 (1C, C-21, C–Cl), 22.42 (1C, C-24, –C–$CH_3$). Anal. calcd for $C_{19}H_{15}ClN_2OS$: C, 64.31; H, 4.26; N, 7.89. Found: C, 64.42; H, 4.35; N, 7.93.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-m-tolylazetidin-2-one (**6c**)*

Yield: 70 %. m.p. 253–255 °C (DMF). IR (KBr) $cm^{-1}$: 2583 (S–H), 1733 (C=O), 1587 (C=C), 1533 (C–N), 767 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.5 (s, 1H, –SH), 8.25 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.13 (dd, $J = 7.8$, 1.4 Hz, 1H, H8, quinoline), 7.83 (dd, $J = 7.3$, 1.6 Hz, 1H, H5, quinoline), 7.66–7.52 (m, 2H, quinoline), 7.47–7.21 (m, 4H, Ar–H), 6.60 (d, $J = 6.7$ Hz, 1H, CH–N at azitidinone ring), 5.91 (d, $J = 6.7$ Hz, 1H), 1.92 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 174.27 (1C, C-8, C–SH), 166.14 (1C, C-20, C=O), 156.41–120.11 (14C, Ar–C), 67.89 (1C, C-12, –Ar.–Azetidinone ring linkage), 62.74 (1C, C-21, C–Cl), 23.45 (1C, C-24, –C–$CH_3$). Anal. calcd for $C_{19}H_{15}ClN_2OS$: C, 64.31; H, 4.26; N, 7.89. Found: C, 64.37; H, 4.33; N, 7.87.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-p-tolylazetidin-2-one (**6d**)*

Yield: 70 %. m.p. 253–255 °C (DMF). IR (KBr) $cm^{-1}$: 2575 (S–H), 1729 (C=O), 1575 (C=C), 1529 (C–N), 763 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.3 (s, 1H, –SH), 8.21 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.07 (dd, $J = 7.6$, 1.4 Hz, 1H, H8, quinoline), 7.81 (dd, $J = 7.2$, 1.4 Hz, 1H, H5, quinoline), 7.61–7.49 (m, 2H, quinoline), 7.41–7.19 (m, 4H, Ar–H), 6.55 (d, $J = 6.6$ Hz, 1H, CH–N at azitidinone ring), 5.81 (d, $J = 6.7$ Hz, 1H), 1.95 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.39 (1C, C-8, C–SH), 163.69 (1C, C-20, C=O), 154.66–127.32 (14C, Ar–C), 67.83 (1C, C-12, –Ar.–Azetidinone ring linkage), 61.72 (1C, C-21, C–Cl), 21.20 (1C, C-24, –C–$CH_3$). Anal. calcd for $C_{19}H_{15}ClN_2OS$: C, 64.31; H, 4.26; N, 7.89. Found: C, 64.25; H, 4.34; N, 7.84.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-(2-nitrophenyl)azetidin-2-one (**6e**)*

Yield: 68 %. m.p. 270–271 °C (DMF). IR (KBr) $cm^{-1}$: 2581 (S–H), 1737 (C=O), 1570 (C=C), 1538 (C–N), 769 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.8 (s, 1H, –SH), 8.17 (d, $J = 1.3$ Hz, 1H, H3, quinoline), 7.95 (dd, $J = 7.8$, 1.5 Hz, 1H, H8, quinoline), 7.79 (dd, $J = 7.4$, 1.6 Hz, 1H, H5, quinoline), 7.67–7.51 (m, 2H, quinoline), 7.43–7.20 (m, 4H, Ar–H), 6.67 (d, $J = 6.7$ Hz, 1H, CH–N at azitidinone ring), 5.85 (d, $J = 6.7$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.67 (1C, C-8, C–SH), 166.28 (1C, C-20, C=O), 154.70–121.15 (13C, Ar–C), 145.35 (1C,

C-13, C–$NO_2$), 69.45 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.35 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{12}ClN_3O_3S$: C, 56.03; H, 3.13; N, 10.89. Found: C, 56.15; H, 3.08; N, 10.94.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-(3-nitrophenyl)azetidin-2-one (**6f**)*

Yield: 63 %. m.p. 260–262 °C (DMF). IR (KBr) $cm^{-1}$: 2585 (S–H), 1733 (C=O), 1580 (C=C), 1533 (C–N), 773 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.6 (s, 1H, –SH), 8.21 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 7.99 (dd, $J = 7.6$, 1.6 Hz, 1H, H8, quinoline), 7.81 (dd, $J = 7.5$, 1.7 Hz, 1H, H5, quinoline), 7.68–7.49 (m, 2H, quinoline), 7.41–7.22 (m, 4H, Ar–H), 6.70 (d, $J = 6.7$ Hz, 1H, CH–N at azitidinone ring), 5.88 (d, $J = 6.7$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.51 (1C, C-8, C–SH), 163.95 (1C, C-20, C=O), 150.62–110.15 (13C, Ar–C), 149.75 (1C, C-13, C–$NO_2$), 67.75 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.75 (1C, C-21, C–Cl of $\beta$-lactum ring), Anal. calcd for $C_{18}H_{12}ClN_3O_3S$: C, 56.03; H, 3.13; N, 10.89. Found: C, 56.12; H, 3.18; N, 10.83.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-(4-nitrophenyl)azetidin-2-one (**6g**)*

Yield: 69 %. m.p. 270–272 °C (DMF). IR (KBr) $cm^{-1}$: 2583 (S–H), 1738 (C=O), 1591 (C=C), 1536 (C–N), 762 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.7 (s, 1H, –SH), 8.19 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 7.97 (dd, $J = 7.7$, 1.5 Hz, 1H, H8, quinoline), 7.77 (dd, $J = 7.4$, 1.6 Hz, 1H, H5, quinoline), 7.66–7.52 (m, 2H, quinoline), 7.40–7.23 (m, 4H, Ar–H), 6.66 (d, $J = 6.6$ Hz, 1H, CH–N at azitidinone ring), 5.84 (d, $J = 6.6$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.35 (1C, C-8, C–SH), 163.75 (1C, C-20, C=O), 154.41–124.62 (13C, Ar–C), 145.15 (1C, C-13, C–$NO_2$), 67.58 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.55 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{12}ClN_3O_3S$: C, 56.03; H, 3.13; N, 10.89. Found: C, 55.09; H, 3.18; N, 10.95.

*3-Chloro-1-(2-chlorophenyl)-4-(2-mercaptoquinolin-3-yl)azetidin-2-one (**6h**)*

Yield: 73 %. m.p. 280–281 °C (DMF). IR (KBr) $cm^{-1}$: 2577 (S–H), 1738 (C=O), 1592 (C=C), 1533 (C–N), 777 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.5 (s, 1H, –SH), 8.25 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.06 (dd, $J = 8.1$, 1.2 Hz, 1H, H8, quinoline), 7.81 (dd, $J = 7.9$, 1.4 Hz, 1H, H5, quinoline), 7.68–7.50 (m, 2H, quinoline), 7.42–7.18 (m, 4H, Ar–H), 6.68 (d, $J = 6.8$ Hz, 1H, CH–N at azitidinone ring), 5.89 (d, $J = 6.4$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.45 (1C, C-8, C–SH), 166.30 (1C, C-20, C=O), 154.89–123.46 (14C, Ar–C), 68.25 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.22 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{12}Cl_2N_2OS$: C, 57.61; H, 3.22; N, 7.46. Found: C, 57.70; H, 3.30; N, 7.51.

*3-Chloro-1-(3-chlorophenyl)-4-(2-mercaptoquinolin-3-yl)azetidin-2-one (**6i**)*

Yield: 70 %. m.p. 255–257 °C (DMF). IR (KBr) $cm^{-1}$: 2580 (S–H), 1733 (C=O), 1595 (C=C), 1540 (C–N), 766 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.1 (s, 1H, –SH), 8.21 (d, $J = 1.3$ Hz, 1H, H3, quinoline), 8.03 (dd, $J = 7.9$, 1.6 Hz, 1H, H8, quinoline), 7.79 (dd, $J = 8.0$, 1.2 Hz, 1H, H5, quinoline), 7.63–7.51 (m, 2H, quinoline), 7.39–7.20 (m, 4H, Ar–H), 6.65 (d, $J = 6.6$ Hz, 1H, CH–N at azitidinone ring), 5.83 (d, $J = 6.3$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.37 (1C, C-8, C–SH), 163.75 (1C, C-20, C=O), 154.23–117.95 (14C, Ar–C), 67.95 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.45 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{12}Cl_2N_2OS$: C, 57.61; H, 3.22; N, 7.46. Found: C, 57.57; H, 3.18; N, 7.55.

*3-Chloro-1-(4-chlorophenyl)-4-(2-mercaptoquinolin-3-yl)azetidin-2-one (**6j**)*

Yield: 73 %. m.p. 253–254 °C (DMF). IR (KBr) $cm^{-1}$: 2583 (S–H), 1735 (C=O), 1576 (C=C), 1539 (C–N), 770 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.4 (s, 1H, –SH), 8.25 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.11 (dd, $J = 8.3$, 1.7 Hz, 1H, H8, quinoline), 7.82 (dd, $J = 8.0$, 1.4 Hz, 1H, H5, quinoline), 7.65–7.49 (m, 2H, quinoline), 7.40–7.18 (m, 4H, Ar–H), 6.70 (d, $J = 6.7$ Hz, 1H, CH–N at azitidinone ring), 5.88 (d, $J = 6.5$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.31 (1C, C-8, C–SH), 163.95 (1C, C-20, C=O), 154.38–118.90 (14C, Ar–C), 67.75 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.55 (1C, C-21, C–Cl). Anal. calcd for $C_{18}H_{12}Cl_2N_2OS$: C, 57.61; H, 3.22; N, 7.46. Found: C, 57.68; H, 3.15; N, 7.38.

*3-Chloro-1-(4-fluorophenyl)-4-(2-mercaptoquinolin-3-yl)azetidin-2-one (**6k**)*

Yield: 71 %. m.p. 266–268 °C (DMF). IR (KBr) $cm^{-1}$: 2589 (S–H), 1738 (C=O), 1593 (C=C), 1541 (C–N), 773 (C–Cl). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.4 (s, 1H, –SH), 8.26 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 8.12 (dd, $J = 8.2$, 1.7 Hz, 1H, H8, quinoline), 7.83 (dd, $J = 8.0$, 1.3 Hz, 1H, H5, quinoline), 7.63–7.50 (m, 2H, quinoline), 7.41–7.21 (m, 4H, Ar–H), 6.68 (d, $J = 6.6$ Hz, 1H, CH–N at azitidinone ring), 5.90 (d, $J = 6.8$ Hz, 1H). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.35 (1C, C-8, C–SH), 163.89 (1C, C-20, C=O), 154.30–115.75 (14C, Ar–C), 68.05 (1C, C-12, –Ar.–Azetidinone ring linkage), 60.75 (1C, C-21,

C–Cl). Anal. calcd for $C_{18}H_{12}ClFN_2OS$: C, 60.25; H, 3.37; N, 7.81. Found: C, 60.37; H, 3.45; N, 7.85.

*3-Chloro-4-(2-mercaptoquinolin-3-yl)-1-(5-methylthiazol-2-yl)azetidin-2-one (**6l**)*

Yield: 58 %. m.p. 291–293 °C (DMF). IR (KBr) $cm^{-1}$: 2585 (S–H), 1731 (C=O), 1539 (C–N), 762 (C–Cl), 650 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.8 (s, 1H, –SH), 8.23 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.11 (dd, $J = 8.1$, 1.5 Hz, 1H, H8, quinoline), 7.79 (dd, $J = 8.1$, 1.3 Hz, 1H, H5, quinoline), 7.61–7.52 (m, 2H, quinoline), 7.20 (d, 1H, Ar–H at thaizole ring), 6.63 (d, $J = 6.5$ Hz, 1H, CH–N at azitidinone ring), 5.88 (d, $J = 6.8$ Hz, 1H), 2.02 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.55 (1C, C-8, C–SH), 160.12 (1C, C-14, C=O), 157.85 (1C, C-20, –N–C at azetidinone-heterocyclic coupling ring), 154.15–126.75 (10C, Ar–C), 64.25 (1C, C-12, –Ar.–Azetidinone ring linkage), 59.50 (1C, C-15, C–Cl),14.45 (1C, C–$CH_3$). Anal. calcd for $C_{16}H_{12}ClN_3OS_2$: C, 53.11; H, 3.34; N, 11.61. Found: C, 53.08; H, 3.41; N, 11.57.

General procedure for preparation of compounds **7a–l**

A mixture of (*Z*)-3-((phenylimino)methyl)quinoline-2-thiol (substituted amine) **5a–l** (0.01 mol) and catalytic amount of zinc chloride (0.05 gm) in DMF was taken in Dean stark apparatus and to it thioglycolic acid (0.02 mol) in DMF was added slowly. The reaction mass was refluxed for 12 h. The DMF was distilled off to get the solid mixture. This was then treated with an excess of 10 % sodium bicarbonate solution to remove excess of thioglycolic acid. The product obtained was filtered, washed several times with water and recrystallized from ethanol.

*2-(2-Mercaptoquinolin-3-yl)-3-phenylthiazolidin-4-one (**7a**)*

Yield: 75 %. m.p. 271–272 °C (DMF). IR (KBr) $cm^{-1}$: 2578 (S–H), 1735 (C=O), 1586 (C=C), 1534 (C–N), 759 (C–Cl), 624 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.9 (s, 1H, –SH), 8.16 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.03 (dd, $J = 7.9$, 1.6 Hz, 1H, H8, quinoline), 7.76 (dd, $J = 7.4$, 1.7 Hz, 1H, H5, quinoline), 7.61–7.51 (m, 2H, quinoline), 7.40–7.21 (m, 5H, Ar–H), 6.42 (d, $J = 6.6$ Hz, 1H, CH–N at thiazolidinone ring), 3.85 (dd, $J = 12.2$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 174.35 (1C, C-20, C=O), 163.88 (1C, C-8, C–SH), 151.23–125.34 (14C, Ar–C), 57.87 (1C, C-12, –Ar. - thiazolidinone ring linkage), 36.92 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{14}N_2OS_2$: C, 63.88; H, 4.17; N, 8.28. Found: C, 63.75; H, 4.25; N, 8.34.

*2-(2-Mercaptoquinolin-3-yl)-3-o-tolylthiazolidin-4-one (**7b**)*

Yield: 71 %. m.p. 263–265 °C (DMF). IR (KBr) $cm^{-1}$: 2583 (S–H), 1739 (C=O of $\beta$-lactum), 1594 (C=C), 1537 (C–N), 763 (C–Cl), 627 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.4 (s, 1H, –SH), 8.24 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 8.05 (dd, $J = 8.0$, 1.5 Hz, 1H, H8, quinoline), 7.82 (dd, $J = 7.8$, 1.6 Hz, 1H, H5, quinoline), 7.65–7.52 (m, 2H, quinoline), 7.41–7.19 (m, 4H, Ar–H), 6.48 (d, $J = 6.6$ Hz, 1H, CH–N at thiazolidinone ring), 3.89 (dd, $J = 12.3$ Hz, 2H, CH–S at thiazolidinone ring), 1.91 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 172.56 (1C, C-8, C–SH), 165.30 (1C, C-20, C=O), 153.91–123.46 (14C, Ar–C), 58.25 (1C, C-12, –Ar.–Azetidinone ring linkage), 35.47 (1C, C-22, –S–C at thiazolidinone ring), 18.14 (1C, C-24, –C–$CH_3$). Anal. calcd for $C_{19}H_{16}N_2OS_2$: C, 64.74; H, 4.58; N, 7.95. Found: C, 64.80; H, 4.63; N, 7.87.

*2-(2-Mercaptoquinolin-3-yl)-3-m-tolylthiazolidin-4-one (**7c**)*

Yield: 66 %. m.p. 245–247 °C (DMF). IR (KBr) $cm^{-1}$: 2578 (S–H), 1731 (C=O), 1582 (C=C), 1533 (C–N), 769 (C–Cl), 633 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.1 (s, 1H, –SH), 8.19 (d, $J = 1.3$ Hz, 1H, H3, quinoline), 8.02 (dd, $J = 8.1$, 1.4 Hz, 1H, H8, quinoline), 7.84 (dd, $J = 7.9$, 1.5 Hz, 1H, H5, quinoline), 7.62–7.49 (m, 2H, quinoline), 7.43–7.20 (m, 4H, Ar–H), 6.52 (d, $J = 6.6$ Hz, 1H, CH–N at thiazolidinone ring), 3.83 (dd, $J = 12.0$ Hz, 2H, CH–S at thiazolidinone ring), 1.95 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 174.21 (1C, C-8, C–SH), 161.87 (1C, C-20, C=O), 153.89–120.85 (14C, Ar–C), 56.45 (1C, C-12, –Ar.–Azetidinone ring linkage), 33.74 (1C, C-22, –S–C at thiazolidinone ring), 19.25 (1C, C-24, –C–$CH_3$).Anal. calcd for $C_{19}H_{16}N_2OS_2$: C, 64.74; H, 4.58; N, 7.95. Found: C, 64.79; H, 4.65; N, 7.90.

*2-(2-Mercaptoquinolin-3-yl)-3-p-tolylthiazolidin-4-one (**7d**)*

Yield: 67 %. m.p. 269–271 °C (DMF). IR (KBr) $cm^{-1}$: 2588 (S–H), 1736 (C=O), 1578 (C=C), 1537 (C–N), 772 (C–Cl), 629 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.5 (s, 1H, –SH), 8.26 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.07 (dd, $J = 8.3$, 1.6 Hz, 1H, H8, quinoline), 7.86 (dd, $J = 7.8$, 1.6 Hz, 1H, H5, quinoline), 7.61–7.51 (m, 2H, quinoline), 7.41–7.19 (m, 4H, Ar–H), 6.49 (d, $J = 6.7$ Hz, 1H, CH–N at thiazolidinone ring), 3.88 (dd, $J = 12.2$ Hz, 2H, CH-S at thiazolidinone ring), 1.90 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 172.56 (1C, C-8, C–SH), 161.87 (1C, C-20, C=O), 151.89–122.85 (14C, Ar–C),

57.45 (1C, C-12, –Ar.–Azetidinone ring linkage), 34.73 (1C, C-22, –S–C at thiazolidinone ring), 20.18 (1C, C-24, –C–$CH_3$). Anal. calcd for $C_{19}H_{16}N_2OS_2$: C, 64.74; H, 4.58; N, 7.95. Found: C, 64.81; H, 4.66; N, 7.85.

*2-(2-Mercaptoquinolin-3-yl)-3-(2-nitrophenyl)thiazolidin-4-one (**7e**)*

Yield: 65 %. m.p. 257–258 °C (DMF). IR (KBr) $cm^{-1}$: 2588 (S–H), 1740 (C=O), 1573 (C=C), 1539 (C–N), 778 (C–Cl), 620 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.7 (s, 1H, –SH), 8.23 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 7.91 (dd, $J = 8.0$, 1.7 Hz, 1H, H8, quinoline), 7.83 (dd, $J = 7.9$, 1.6 Hz, 1H, H5, quinoline), 7.63–7.54 (m, 2H, quinoline), 7.45–7.22 (m, 4H, Ar–H), 6.51 (d, $J = 6.7$ Hz, 1H, CH–N at thiazolidinone ring), 3.94 (dd, $J = 12.4$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 177.31 (1C, C-8, C–SH), 164.82 (1C, C-20, C=O), 151.65–120.78 (14C, Ar–C), 59.46 (1C, C-12, –Ar.–Azetidinone ring linkage), 36.57 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}N_3O_3S_2$: C, 56.38; H, 3.42; N, 10.96. Found: C, 56.45; H, 3.49; N, 10.88.

*2-(2-Mercaptoquinolin-3-yl)-3-(3-nitrophenyl)thiazolidin-4-one (**7f**)*

Yield: 60 %. m.p. 275–277 °C (DMF). IR (KBr) $cm^{-1}$: 2593 (S–H), 1737 (C=O), 1579 (C=C), 1537 (C–N), 774 (C–Cl), 619 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.9 (s, 1H, –SH), 8.27 (d, $J = 1.3$ Hz, 1H, H3, quinoline), 7.84 (dd, $J = 7.9$, 1.6 Hz, 1H, H8, quinoline), 7.82 (dd, $J = 7.8$, 1.5 Hz, 1H, H5, quinoline), 7.62–7.51 (m, 2H, quinoline), 7.43–7.19 (m, 4H, Ar–H), 6.60 (d, $J = 6.5$ Hz, 1H, CH–N at thiazolidinone ring), 3.91 (dd, $J = 12.1$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 175.16 (1C, C-8, C–SH), 162.95 (1C, C-20, C=O), 149.62–115.19 (14C, Ar–C), 57.85 (1C, C-12, –Ar.–Azetidinone ring linkage), 34.78 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}N_3O_3S_2$: C, 56.38; H, 3.42; N, 10.96. Found: C, 56.30; H, 3.35; N, 10.91.

*2-(2-Mercaptoquinolin-3-yl)-3-(4-nitrophenyl)thiazolidin-4-one (**7g**)*

Yield: 63 %; m.p. 249–251 °C (DMF). IR (KBr) $cm^{-1}$: 2593 (S–H), 1740 (C=O), 1575 (C=C), 1538 (C–N), 780 (C–Cl), 627 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.6 (s, 1H, –SH), 8.20 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 7.90 (dd, $J = 7.9$, 1.7 Hz, 1H, H8, quinoline), 7.80 (dd, $J = 7.9$, 1.6 Hz, 1H, H5, quinoline), 7.63–7.54 (m, 2H, quinoline), 7.41–7.20 (m, 4H, Ar–H), 6.58 (d, $J = 6.6$ Hz, 1H, CH–N at thiazolidinone ring), 3.93 (dd, $J = 12.3$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 174.57 (1C, C-8, C–SH), 164.53 (1C, C-20, C=O), 148.22–119.58 (14C, Ar–C), 58.84 (1C, C-12, –Ar.–Azetidinone ring linkage), 35.74 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}N_3O_3S_2$: C, 56.38; H, 3.42; N, 10.96. Found: C, 56.43; H, 3.51; N, 10.85.

*3-(2-Chlorophenyl)-2-(2-mercaptoquinolin-3-yl)thiazolidin-4-one (**7h**)*

Yield: 59 %. m.p. 263–265 °C (DMF). IR (KBr) $cm^{-1}$: 2587 (S–H), 1736 (C=O), 1591 (C=C), 1536 (C–N), 773 (C–Cl), 630 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 12.1 (s, 1H, –SH), 8.15 (d, $J = 1.4$ Hz, 1H, H3, quinoline), 8.11 (dd, $J = 8.2$, 1.7 Hz, 1H, H8, quinoline), 7.85 (dd, $J = 7.7$, 1.8 Hz, 1H, H5, quinoline), 7.61–7.55 (m, 2H, quinoline), 7.43–7.22 (m, 4H, Ar–H), 6.49 (d, $J = 6.7$ Hz, 1H, CH–N at thiazolidinone ring), 3.89 (dd, $J = 11.9$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 172.75 (1C, C-8, C–SH), 162.27 (1C, C-20, C=O), 150.22–120.58 (14C, Ar–C), 57.26 (1C, C-12, –Ar.–Azetidinone ring linkage), 34.72 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}ClN_2OS_2$: C, 57.98; H, 3.51; N, 7.51. Found: C, 57.90; H, 3.59; N, 7.41.

*3-(3-Chlorophenyl)-2-(2-mercaptoquinolin-3-yl)thiazolidin-4-one (**7i**)*

Yield: 55 %. m.p. 286–288 °C (DMF). IR (KBr) $cm^{-1}$: 2575 (S–H), 1739 (C=O), 1587 (C=C), 1538 (C–N), 780 (C–Cl), 626 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 12.3 (s, 1H, –SH), 8.20 (d, $J = 1.5$ Hz, 1H, H3, quinoline), 8.13 (dd, $J = 8.0$, 1.6 Hz, 1H, H8, quinoline), 7.87 (dd, $J = 7.8$, 1.6 Hz, 1H, H5, quinoline), 7.64–7.53 (m, 2H, quinoline), 7.41–7.20 (m, 4H, Ar–H), 6.46 (d, $J = 6.7$ Hz, 1H, CH–N at thiazolidinone ring), 3.85 (dd, $J = 11.9$ Hz, 2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 170.85 (1C, C-8, C–SH), 160.45 (1C, C-20, C=O), 152.47–119.68 (14C, Ar–C), 56.87 (1C, C-12, –Ar.–Azetidinone ring linkage), 35.78 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}ClN_2OS_2$: C, 57.98; H, 3.51; N, 7.51. Found: C, 57.93; H, 3.45; N, 7.58.

*3-(4-Chlorophenyl)-2-(2-mercaptoquinolin-3-yl)thiazolidin-4-one (**7j**)*

Yield: 60 %. m.p. 260–262 °C (DMF). IR (KBr) $cm^{-1}$: 2575 (S–H), 1733 (C=O), 1593 (C=C), 1536 (C–N), 773 (C–Cl), 629 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.9 (s, 1H, –SH), 8.15 (d, $J = 1.6$ Hz, 1H, H3, quinoline), 8.07 (dd, $J = 8.2$, 1.5 Hz, 1H, H8, quinoline), 7.79 (dd, $J = 7.6$, 1.4 Hz, 1H, H5, quinoline), 7.62–7.54 (m, 2H, quinoline), 7.43–7.19 (m, 4H, Ar–H), 6.49 (d, $J = 6.8$ Hz, 1H, CH–N at thiazolidinone ring), 3.89 (dd, $J = 11.7$ Hz,

2H, CH–S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 173.24 (1C, C-8, C–SH), 162.28 (1C, C-20, C=O), 150.47–122.68 (14C, Ar–C), 58.48 (1C, C-12, –Ar.–Azetidinone ring linkage), 36.75 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}ClN_2OS_2$: C, 57.98; H, 3.51; N, 7.51. Found: C, 57.92; H, 3.55; N, 7.47.

*3-(4-Fluorophenyl)-2-(2-mercaptoquinolin-3-yl)thiazolidin-4-one (**7k**)*

Yield: 59 %. m.p. 274–277 °C (DMF). IR (KBr) cm$^{-1}$: 2575 (S–H), 1738 (C=O), 1589 (C=C), 1536 (C–N), 765 (C–Cl), 617 (C–S–C); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 12.2 (s, 1H, –SH), 8.19 (d, $J$ = 1.7 Hz, 1H, H3, quinoline), 8.13 (dd, $J$ = 8.3, 1.4 Hz, 1H, H8, quinoline), 7.83 (dd, $J$ = 7.7, 1.5 Hz, 1H, H5, quinoline), 7.64–7.52 (m, 2H, quinoline), 7.42–7.21 (m, 4H, Ar–H), 6.51 (d, $J$ = 6.6 Hz, 1H, CH–N at thiazolidinone ring), 3.91 (dd, $J$ = 11.9 Hz, 2H, CH-S at thiazolidinone ring). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 172.92 (1C, C-8, C–SH), 161.37 (1C, C-20, C=O), 151.74–121.46 (14C, Ar–C), 57.88 (1C, C-12, –Ar.–Azetidinone ring linkage), 36.22 (1C, C-22, –S–C at thiazolidinone ring). Anal. calcd for $C_{18}H_{13}FN_2OS_2$: C, 60.65; H, 3.68; N, 7.86; Found: C, 60.73; H, 3.74; N, 7.77.

*2-(2-Mercaptoquinolin-3-yl)-3-(5-methylthiazol-2-yl)thiazolidin-4-one(**7l**)*

Yield: 55 %. m.p. 287–290 °C (DMF). IR (KBr) cm$^{-1}$: 2583 (S–H), 1741 (C=O), 1583 (C=C), 1539 (C–N), 778 (C–Cl), 627 (C–S–C). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 11.7 (s, 1H, –SH), 8.21 (d, $J$ = 1.5 Hz, 1H, H3, quinoline), 8.07 (dd, $J$ = 8.3, 1.6 Hz, 1H, H8, quinoline), 7.81 (dd, $J$ = 7.9, 1.4 Hz, 1H, H5, quinoline), 7.62–7.54 (m, 2H, quinoline), 7.22 (d, 1H, Ar–H at thaizole ring), 6.49 (d, $J$ = 6.5 Hz, 1H, CH–N at azitidinone ring), 3.87 (dd, $J$ = 12.4 Hz, 2H, CH–S at thiazolidinone ring), 2.13 (s, 3H, Ar–$CH_3$). $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 176.55 (1C, C-8, C–SH), 162.12 (1C, C-14, C=O), 157.85 (1C, C-20, –N–C at azetidinone-heterocyclic coupling ring), 154.15–126.75 (10C, Ar–C), 58.78 (1C, C-12, –Ar.–Azetidinone ring linkage), 59.50 (1C, C-15, C–Cl), 14.45 (1C, C–$CH_3$). Anal. calcd for $C_{16}H_{13}N_3OS_3$: C, 53.46; H, 3.64; N, 11.69. Found: C, 53.55; H, 3.58; N, 11.60.

## Conclusion

In summary, we have developed a novel, efficient and potent quinoline-based azetidinone and thiazolidinone analogues. Quinoline nucleus is one of the active constituents present in many standard drugs, and is known to increase the pharmacological activities of the molecule. The presence of substituted amines is also an instrumental in contributing the net biological activity. In brief, high potency has been observed with the final scaffolds in the form of azetidinones and thiazolidinones bearing various amines containing halogen(s) such as chloro or fluoro and nitro functional groups. The final results indicated that quinoline-based thiazolidinones are more efficious antimicrobial agents compared to quinoline-based azetidinones analogues. Hence, there is enough scope for further study in developing such compounds as a good lead activity. Overall conclusion placed for synthesized compounds is that most of the compounds shown moderate to promising activity as compared to standard drug against all representative panel of bacterial and fungal strains.

**Acknowledgments** The authors are thankful to Applied Chemistry Department of S. V. National Institute of Technology, Surat for encouragement and facilities. The authors wish to offer their deep gratitude to Centre of Excellence, Vapi, India for carrying out $^1$H NMR and $^{13}$C NMR analysis.

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