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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis and antimicrobial activity of 5-chloroindoline-2,3-dione derivatives

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Abstract A series of 3-(5-chloro-2-oxoindolin-3-ylideneamino)-2-arylthiazolidin-4-ones **4a–k** and 5-chloro-3-(3-chloro-2-oxo-4-arylazetidin-1-ylimino)indolin-2-ones **5a–k** was synthesized. The structures of final compounds were confirmed by analytical (C, H, N) and spectral (FT-IR, ^{1}H NMR, ^{13}C NMR and Mass) data. The synthesized compounds were screened for possible antibacterial and antifungal activity. Compounds **4c**, **4f**, **4g**, **4h, 4i**, **4j**, **5c**, **5f**, **5g**, **5h**, **5i** and **5j** showed substantially significant activity.

Keywords 5-Chloroindoline-2,3-dione · Azetidinone · Thiazolidinone · Antibacterial and antifungal activity

Introduction

Isatin derivatives have been found to possess potent wide spectrum of activities like antibacterial, antifungal (Bondock *et al.*, 2008; Gupta and Narayana, 1997; Pandeya *et al.*, 1999; Sridhar *et al.*, 2001), antitubercular (Aboul-Fadl *et al.*, 2003; Karali *et al.*, 2007), anticonvulsant (Verma *et al.*, 2004; Sridhar *et al.*, 2002), anticancer (Vine *et al.*, 2007) and antioxidant (Andreani *et al.*, 2010). The 2-azetidinone (β-lactam) ring system is a common structural feature in number of broad spectrum β-lactam antibiotics like penicillins and cephalosporins which have been widely used as chemotherapeutic agents to treat bacterial infections and diseases. These molecules operate by forming a covalent adduct with membrane-bound bacterial transpeptidases, which are also known as penicillin binding proteins (PBPs), involved in the biosynthesis of cell wall. These therapeutic agents prevent the construction of cell wall and eventually lead to cell lysis and death. Moreover, due to their β-lactamase inhibitory action, 2-azetidinone-based heterocycles represent an attractive target of contemporary organic synthesis. A large numbers of 2-azetidinones (Arnould *et al.*, 1992; Halve *et al.*, 2007; Keri *et al.*, 2009) were reported to possess antibacterial and antifungal activity. The 4-thiazoldinone nucleus has drawn many attentions due to its various activities like antimicrobial (Vicini *et al.*, 2008), anti-HIV (Chen *et al.*, 2009; Rao *et al.*, 2004; Rawal *et al.*, 2005) anticancer (Abdel-Aziz *et al.*, 2010; Lv *et al.*, 2010) and antihypertensive (Bhandari *et al.*, 2009).

Various chemotherapeutic drugs are in use but due to increase in microbial resistance against these drugs, there is a need to develop new, potent and fast-acting antimicrobial drugs. In the light of these observations, it was planned to synthesize a series of isatin derivatives by incorporating the azetidinone/thiazolidinone moiety at third position of isatin nucleus with an aim to get better antibacterial as well as antifungal activity.

Results and discussion

Chemistry

The synthetic routes of compounds are outlined in Scheme 1. The compound 5-chloroindoline-2,3-dione **1** was prepared

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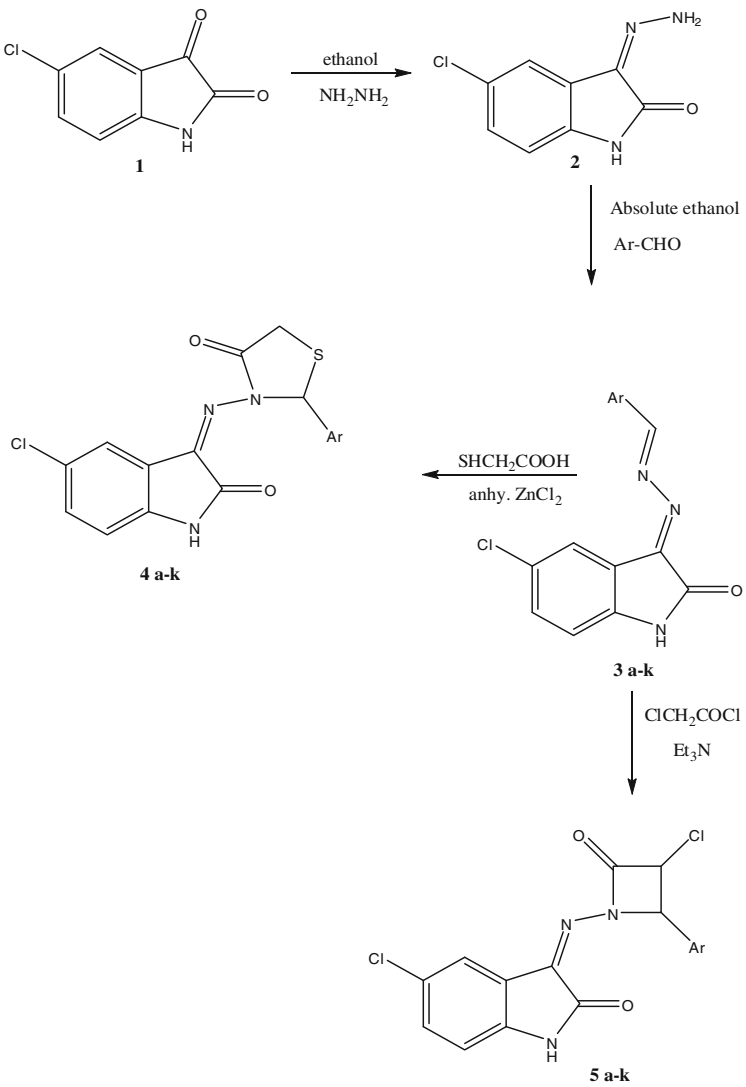

Scheme 1 **3a–k**, **4a–k** and **5a–k**. Ar = phenyl,2-chlorophenyl, 4-chlorophenyl,3-methoxyphenyl,2-hydorxyphenyl, 4-hydorxyphenyl,4-dimethylaminophenyl, 4-methoxyphenyl,4-fluorophenyl,4-nitorphenyl and 2-furan

according to reported method (Marvel and Hiers, 1941). The condensation of 5-chloroindoline-2,3-dione **1** with hydrazine hydrate in ethanol afforded 5-chloro-3-hydrazonoindolin-2-one **2** (Khan *et al.*, 2002, 2009). Compound **2** on further reaction with different substituted aromatic aldehydes in presence of 2–3 drops of glacial acetic acid in ethanol yielded the corresponding 5-chloro-3-[(arylidene)hydrazono]indoline-2-ones **3a–3k**. Compounds **3a–3k**, further undergoes cyclization with thioglycolic acid in presence of anhydrous $ZnCl_2$ and with chloroacetylchloride in presence of triethylamine (Et_3N) to afford 3-(5-chloro-2-oxoindolin-3-ylideneamino)-2-arylthiazolidin-4-ones **4a–4k** (Agarwal *et al.*, 2006) and 5-chloro-3-(3-chloro-2-oxo-4-arylazetidin-1-ylimino)indolin-2-ones **5a–5k** (Bhati and Kumar, 2008), respectively.

The thiazolidi-4-ones and azetidi-2-ones are formed by cycloaddition mechanism (Soleiman, 2011). The formation of compounds **3a–k** was evidenced by appearance of a band between 1675 and 1703 cm^{-1} (N=CH) in the IR spectrum and appearance of a singlet between δ 8.58–9.1 for one proton of –N=CH–Ar in the ^1H NMR spectra also supports their structures. Cycloaddition of thioglycolic acid to **3a–3k** resulted into compounds **4a–4k** which was confirmed by the presence of a band between 1760 and 1771 cm^{-1} (C=O of β-thialactum ring) in the IR spectra and a singlet in between δ 3.1–3.5 of two protons of CH_2 of thiazolidinone ring and 4.3–4.8 of –CH–Ar in the ^1H NMR spectra. Cycloaddition of chloroacetylchloride to **3a–3k** resulted into compounds **5a–5k** which was confirmed by the presence of a band between 1745 and 1760 cm^{-1} (C=O of β-lactam ring) in the IR spectra and a singlet in between δ 4.25–4.9 of –CH–Cl and 5.2–5.5 of –CH–Ar in the ^1H NMR spectra.

Antimicrobial activity

All the synthesized compounds were screened for their possible antibacterial and antifungal activities by

determining minimum inhibitory concentrations (MICs) in μg ml^{-1} against selected strains. The MICs was determined by broth dilution method (Srinivas *et al.*, 2006). The MIC was determined for each compound along with ciprofloxacin as standard control and the results are presented in Tables 1 and 2. The MIC values of 12 derivatives against tested organisms exhibited significant activity with a degree of variation. It was found that 4-thiazolidinone derivatives of 5-chloroisatin displayed substantially significant activity: compound **4c** against *S. hominis*, *B. pumilus*, *B. cereus*, *S. typhi*, *E. coli* and *P. aeroginosa*; **4f** against *S. epiderimidis*, *S. hominis*, *B. pumilus*, *P. vulgaris*, *S. typhi*, *K. pneumonia* and *P. aeroginosa*; **4g** against *S. aureus*, *S. hominis*, *B. pumilus*, *P. mirabilis* and *S. typhi*; **4h** against *B. subtilis*, *S. epidermidis*, *P. mirabilis*, *S. typhi* and *K. pneumonia*; **4i** against *S. epiderimidis*, *S. hominis*, *B. pumilus*, *B. cereus*, *S. typhi* and *P. aeroginosa*; **4j** against *M. luteus*, *S. aureus*, *S. hominis*, *S. typhi* and *P. aeroginosa*.

In case of 2-azetidinone derivatives of 5-chloroisatin, the substantially significant activity is exhibited by: compound **5c** against *B. subtilis*, *S. hominis*, *B. pumilus*, *P. vulgaris*, *S. typhi* and *K. pneumonia*; **5f** against *B. subtilis*, *S. epiderimidis*, *B. pumilus*, *B. cereus*, *P. vulgaris*, *P. mirabilis*, *S. typhi*, *E. coli* and *P. aeroginosa*; **5g** against *S. epiderimidis*, *B. pumilus*, *P. vulgaris*, *S. typhi*, *K. pneumonia*, *E. coli* and *P. aeroginosa*; **5h** against *S. epiderimidis*, *M. luteus*, *B. pumilus*, *B. cereus*, *S. typhi*, *K. pneumonia*, *E. coli* and *P. aeroginosa*; **5i** against *B. subtilis*, *S. hominis*, *P. mirabilis* and *S. typhi*; **5j** against *B. subtilis*, *M. luteus*, *B. pumilus*, *B. cereus*, *P. vulgaris*, *P. mirabilis*, *S. typhi*, *K. pneumonia* and *P. aeroginosa*.

The antifungal activity (MIC) of all the synthesized compounds was determined by using clotrimazole as standard control. From the series of 4-thiazolidinone, derivatives **4c**, **4f**, **4g**, **4h**, **4i** and **4j** exhibited substantially significant activity against *A. niger*, *A. Awamori*, *C. albicans*, *A. alternate*, *M. canis*, *R. solani*, *T. longiformis*, *A. flavus*, *F. solani*, *T. viride*, *A. flavus* and *A. fumigatus.* Also, the compounds **5c**, **5f**, **5g**, **5h**, **5i** and **5j** of 2-azetidinone series showed substantially significant activity against *A. niger*, *A. Awamori*, *C. albicans*, *A. alternate*, *M. canis*, *R. solani*, *T. longiformis*, *A. flavus*, *F. solani*, *T. viride*, *A. flavus* and *A. fumigatus.* The compounds **4a**, **4d**, **4k**, **5a**, **5d** and **5k** showed significant activity and **4b**, **4e**, **5b** and **5e** are found to be inactive against all screened strains of bacteria and fungi.

Conclusions

In this study, we report synthesis and characterization of a series of 3-(5-chloro-2-oxoindolin-3-ylideneamino)-2-arylthiazolidin-4-one and 5-chloro-3-(3-chloro-2-oxo-4-arylazetidin-1-ylimino)indolin-2-one from 5-chloro-3-[(arylidene)hydrazono]indoline-2-one although the synthesis of spirothiazolidinone (Bhambi *et al.*, 2009; Dandia *et al.*, 2006) and spiroazetidinone (Dandia *et al.*, 2007; Singh and Luntha, 2009) derivatives of isatin are reported previously. The activity data reveals that the compounds **4c**, **4f**, **4g**, **4h**, **4i**, **4j**, **5c**, **5f**, **5g**, **5h**, **5i** and **5j** having electron withdrawing as well as electron releasing substitution at fourth position of the phenyl ring exhibits good antibacterial as well as antifungal activities. The compounds **4d** and **5d** having electron releasing substituents at third position of the phenyl ring exhibits moderate activity. In compounds **4b**, **4e**, **5b** and **5e** electron withdrawing substituents at second position of phenyl ring are found to be inactive. In conclusion, the substitution at the fourth position may enhance activity and substitution at second position may decrease the activity.

Experimental protocols

General

All reagents and solvents used in study are of analytical grade and have been procured locally. The progress of the reaction is monitored by TLC and the products are purified through recrystallization. The melting points (m. p.) were determined in one-end-open capillary method and are uncorrected. The CATA-2R microwave was used for microwave assisted reaction. IR spectra were recorded on Shimadzu FT-IR 8400-S spectrophotometer using potassium bromide (KBr) pellet. The ^{1}H NMR spectra were acquired on Varian AMX 300 NMR instrument using $CDCl_3$ or DMSO-d_6 as the solvent and TMS as the internal reference (chemical shifts in δ, ppm); ^{13}C NMR was performed on Varian AMX 300 (100 MHz) spectrometer using solutions in $CDCl_3$ or DMSO-d_6 and mass spectra were acquired on API 2000 spectrometer. The elemental analysis (C, H, N) of compounds was performed on Elementar Vario EL III elemental analyzer.

*General procedure for the synthesis of 5-chloro-3-[(arylidene)hydrazono] indoline-2-one (**3a–k**)*

5-Chloro-3-hydrazonoindolin-2-one (**2**, 0.1 mol), various substituted aromatic aldehydes (0.1 mol) and two drops of glacial acetic acid in 50 ml absolute alcohol was refluxed for 2 h. The reaction mixture was cooled at room temperature. The solid mass thus obtained was recrystallized from suitable solvent to obtain compounds **3a–k**.

*3-(Benzylidenehydrazono)-5-chloroindolin-2-one (**3a**)* Yield 82% (ethanol); m. p. 268–270°C. IR (KBr, cm^{-1}):

Table 1 Antibacterial activity of the compounds: MIC in μg ml^{-1}

Comp. code	Name of microorganism (MIC in μg ml^{-1})												
	B. subtilis	*S. epidermidis*	*M. luteus*	*S. aureus*	*S. hominis*	*B. pumilus*	*B. cereus*	*P. vulgaris*	*P. mirabilis*	*S. typhi*	*K. pneumonia*	*E. coli*	*P. aeroginosa*
4a	75.0	37.5	37.5	37.5	75.0	75.0	37.5	75.0	75.0	75.0	37.5	37.5	37.5
4b	300	150	300	300	150	150	150	300	300	150	150	150	150
4c	37.5	18.75	18.75	18.75	9.37	9.37	9.37	37.5	18.75	9.37	18.75	9.37	9.37
4d	75.0	75.0	75.0	37.5	37.5	75.0	75.0	37.5	37.5	75.0	37.5	75.0	75.0
4e	150	300	150	300	150	150	150	150	300	150	300	300	300
4f	18.75	9.37	18.75	18.75	9.37	9.37	18.75	9.37	18.75	9.37	9.37	18.75	9.37
4g	18.75	18.75	18.75	9.37	9.37	9.37	18.75	18.75	9.37	9.37	18.75	18.75	18.75
4h	9.37	9.37	18.75	18.75	18.75	18.75	18.75	37.5	9.37	9.37	9.37	18.75	18.75
4i	18.75	9.37	18.75	18.75	9.37	9.37	9.37	18.75	18.75	9.37	18.75	18.75	9.37
4j	37.5	18.75	9.37	9.37	9.37	18.75	18.75	37.5	18.75	18.75	9.37	18.75	9.37
4k	37.5	75.0	75.0	75.0	37.5	37.5	75.0	75.0	75.0	37.5	75.0	75.0	75.0
5a	37.5	37.5	37.5	75.0	75.0	37.5	37.5	37.5	37.5	75.0	37.5	37.5	37.5
5b	150	150	150	300	300	300	300	150	300	300	300	150	300
5c	9.37	18.75	18.75	18.75	9.37	9.37	18.75	9.37	18.75	9.37	9.37	18.75	18.75
5d	75.0	37.5	37.5	75.0	75.0	75.0	37.5	75.0	75.0	75.0	37.5	75.0	37.5
5e	300	300	150	150	300	300	300	150	150	300	300	150	300
5f	9.37	9.37	18.75	18.75	18.75	9.37	9.37	9.37	9.37	9.37	18.75	9.37	9.37
5g	18.75	9.37	18.75	18.75	18.75	9.37	18.75	9.37	18.75	9.37	9.37	9.37	9.37
5h	18.75	9.37	9.37	18.75	18.75	9.37	9.37	18.75	18.75	9.37	9.37	9.37	9.37
5i	9.37	18.75	18.75	18.75	9.37	18.75	18.75	18.75	9.37	9.37	18.75	18.75	18.75
5j	9.37	18.75	9.37	18.75	18.75	9.37	9.37	9.37	9.37	9.37	9.37	18.75	9.37
5k	75.0	75.0	37.5	37.5	37.5	37.5	37.5	37.5	37.5	75.0	75.0	37.5	37.5
Standard*	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7	4.7

Standard*—ciprofloxacin

MIC minimum inhibitory concentration

Table 2 Antifungal activity of the compounds: MIC in μg ml^{-1}

Comp. code	Name of microorganism (MIC in μg ml^{-1})										
	A. niger	*A. awamori*	*C. albicans*	*A. alternate*	*M. canis*	*R. Solani*	*T. longiformis*	*F. solani*	*T. viride*	*A. flavus*	*A. fumigatus*
4a	18.75	18.75	9.37	37.5	37.5	37.5	18.75	18.75	37.5	37.5	18.75
4b	75.0	150	150	150	75.0	75.0	150	150	75.0	150	150
4c	4.68	9.37	4.68	4.68	4.68	9.37	4.68	9.37	9.37	4.68	4.68
4d	37.5	37.5	18.75	18.75	18.75	18.75	37.5	18.75	18.75	18.75	37.5
4e	150	150	75.0	75.0	75.0	150	150	150	150	75.0	150
4f	4.68	4.68	4.68	9.37	9.37	9.37	4.68	4.68	4.68	9.37	4.68
4g	4.68	9.37	9.37	4.68	9.37	4.68	4.68	4.68	4.68	4.68	4.68
4h	4.68	4.68	4.68	9.37	9.37	9.37	4.68	4.68	4.68	9.37	4.68
4i	9.37	9.37	9.37	9.37	9.37	4.68	4.68	4.68	4.68	9.37	4.68
4j	4.68	9.37	9.37	4.68	4.68	9.37	4.68	9.37	9.37	4.68	4.68
4k	37.5	37.5	18.75	37.5	37.5	18.75	18.75	37.5	37.5	37.5	18.75
5a	18.75	37.5	37.5	18.75	37.5	18.75	37.5	18.75	18.75	18.75	37.5
5b	150	150	75.0	150	75.0	150	150	150	150	150	150
5c	4.68	4.68	4.68	9.37	9.37	9.37	4.68	4.68	4.68	9.37	4.68
5d	37.5	37.5	18.75	18.75	37.5	18.75	18.75	37.5	37.5	18.75	18.75
5e	75.0	150	75.0	150	150	150	150	75.0	150	150	150
5f	4.68	4.68	4.68	4.68	4.68	4.68	4.68	9.37	4.68	4.68	4.68
5g	9.37	9.37	4.68	4.68	4.68	9.37	4.68	9.37	4.68	4.68	4.68
5h	4.68	4.68	4.68	9.37	9.37	9.37	4.68	4.68	4.68	9.37	4.68
5i	4.68	4.68	4.68	4.68	9.37	9.37	9.37	9.37	9.37	4.68	9.37
5j	4.68	9.37	4.68	4.68	4.68	9.37	9.37	9.37	9.37	4.68	9.37
5k	18.75	37.5	18.75	37.5	37.5	37.5	18.75	37.5	37.5	37.5	18.75
Standard*	2.34	2.34	0.58	2.34	1.17	1.17	2.34	1.17	1.17	2.34	2.34

Standard*—clotrimazole

MIC minimum inhibitory concentration

3246 (NH), 3023 (CH aromatic), 1685 (C=O), 1616 (C=N), 752 (C–Cl); ^{1}H NMR ($CDCl_3$) δ in ppm: 6.8–6.9 (d, 1H, Ar–*H*), 7.4–7.8 (m, 7H, Ar–*H*), 8.7 (s, 1H, –N=C*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR ($CDCl_3$) δ in ppm: 169.1, 149.5, 145.8, 143.2, 141.1, 138.4, 135.6, 133.7, 130.8, 128.2, 125.9, 123.5, 119.1. Anal. Calcd. for $C_{15}H_{10}ClN_3O$: C 63.50, H 3.55, N 14.81; Found: C 63.57, H 3.47, N 14.89%.

*5-Chloro-3-[(2-chlorobenzylidene)hydrazono]indolin-2-one (**3b**)* Yield 78% (ethanol); m. p. 236–238°C. IR (KBr, cm^{-1}): 3250 (NH), 3064 (CH aromatic), 1703 (C=O), 1617 (C=N), 743 (C–Cl); ^{1}H NMR ($CDCl_3$) δ in ppm: 6.9–7.0 (d, 1H, Ar–*H*), 7.2–7.4 (m, 5H, Ar–*H*), 8.25–8.35 (m, 1H, Ar–*H*), 9.1 (s, 1H, –N=C*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR ($CDCl_3$) δ in ppm: 169.0, 151.1, 146.5, 144.2, 142.2, 140.1, 138.0, 136.1, 133.6, 131.8, 129.7, 127.8, 125.5, 123.1, 119.2. Anal. Calcd. for $C_{15}H_9Cl_2N_3O$: C 56.63, H 2.85, N 13.21; Found: C 56.71, H 2.80, N 13.27%.

*5-Chloro-3-[(4-chlorobenzylidene)hydrazono]indolin-2-one (**3c**)* Yield 85% (ethanol); m. p. 185–187°C. IR (KBr, cm^{-1}): 3280 (NH), 3068 (CH aromatic), 1685 (C=O), 1623 (C=N), 755 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 6.9–7.0 (s, 1H, Ar–*H*), 7.35–7.95 (m, 6H, Ar–*H*), 8.58 (s, 1H, –N=C*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 169.2, 149.3, 142.2, 140.5, 138.6, 136.5, 134.8, 132.3, 130.6, 129.2, 126.4, 123.9, 118.9. Anal. Calcd. for $C_{15}H_9Cl_2N_3O$: C 56.63, H 2.85, N 13.21; Found: C 56.75, H 2.79, N 13.24%.

*5-Chloro-3-[(3-methoxybenzylidene)hydrazono]indolin-2-one (**3d**)* Yield 87% (methanol); m. p. 198–200°C. IR (KBr, cm^{-1}): 3242 (NH), 3065 (CH aromatic), 1684 (C=O), 1640 (C=N), 1267 (C–O–C), 745 (C–Cl); ^{1}H NMR ($CDCl_3$) δ in ppm: 3.9 (s, 3H, –OCH_3), 6.85–7.57 (m, 5H, Ar–*H*), 8.65 (s, 1H, –N=C*H*), 11.2 (s, 1H, Het-N*H*); ^{13}C NMR ($CDCl_3$) δ in ppm: 169.4, 160.7, 150.8, 142.2, 139.7, 136.8, 134.5, 131.6, 129.1, 127.0, 124.7, 120.8, 118.2,

116.1, 111.0, 54.9. Anal. Calcd. for $C_{16}H_{12}ClN_3O_2$: C 61.25, H 3.86, N 13.39; Found: C 61.33, H 3.75, N 13.34%.

*5-chloro-3-[(2-hydroxybenzylidene)hydrazono]indolin-2-one (**3e**)* Khan *et al.* (2009).

*5-Chloro-3-[(4-hydroxybenzylidene)hydrazono]indolin-2-one (**3f**)* Yield 88% (ethanol); m. p. 238–240°C. IR (KBr, cm^{-1}): 3410 (Ar–OH), 3290 (NH), 3055 (CH aromatic), 1675 (C=O), 1639 (C=N), 751 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 6.7–6.8 (d, 1H, Ar–*H*), 6.8–6.9 (d, 2H, Ar–*H*), 7.6–7.8 (m, 4H, Ar–*H*), 8.58 (s, 1H, –N=C*H*), 10.1 (s, 1H O*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 169.2, 161.0, 149.6, 141.1, 138.1, 134.9, 132.7, 130.8, 127.5, 125.5, 123.0, 119.8, 116.1. Anal. Calcd. for $C_{15}H_{10}ClN_3O_2$: C 60.11, H 3.36, N 14.02; Found: C 60.15, H 3.47, N 14.13%.

*5-Chloro-3-[(4-dimethylaminobenzylidene)hydrazono]indolin-2-one (**3g**)* Yield 83% (ethanol); m. p. 228–230°C. IR (KBr, cm^{-1}): 3306 (NH), 3077 (CH aromatic), 2846 (CH aliphatic), 1688 (C=O), 1626 (C=N), 748 (C–Cl); ^{1}H NMR ($CDCl_3$) δ in ppm: 2.4 (s, 6H, –N(CH_3)$_2$), 6.7–6.8 (d, 2H, Ar–*H*), 6.9–7.0 (d, 1H, Ar–*H*), 7.58–7.8 (m, 4H, Ar–*H*), 8.6 (s, 1H, –N=C*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR ($CDCl_3$) δ in ppm: 169.9, 153.4, 149.4, 140.2, 138.1, 136.0, 133.7, 131.8, 129.5, 125.4, 122.1, 119.3, 111.8, 40.1. Anal. Calcd. for $C_{17}H_{15}ClN_4O$: C 62.48, H 4.63, N 17.15; Found: C 62.55, H 4.52, N 17.20%.

*5-Chloro-3-[(4-methoxybenzylidene)hydrazono]indolin-2-one (**3h**)* Yield 90% (ethanol); m. p. 243–244°C. IR (KBr, cm^{-1}): 3310 (NH), 3061 (CH aromatic), 1695 (C=O), 1625 (C=N), 1251 (C–O–C), 750 (C–Cl); ^{1}H NMR ($CDCl_3$) δ in ppm: 3.85 (s, 3H, –OCH_3), 6.79–6.85 (d, 1H, Ar–*H*), 6.92–7.0 (d, 2H, Ar–*H*), 7.75–7.98 (m, 4H, Ar–*H*), 8.6 (s, 1H, –N=C*H*), 11.2 (s, 1H, Het-N*H*); ^{13}C NMR ($CDCl_3$) δ in ppm: 169.5, 162.6, 150.2, 142.6, 140.2, 137.7, 135.3, 132.7, 130.0, 127.2, 124.5, 119.6, 114.5, 55.9. Anal. Calcd. for $C_{16}H_{12}ClN_3O_2$: C 61.25, H 3.86, N 13.39; Found: C 61.33, H 3.81, N 13.46%.

*5-chloro-3-[(4-fluorobenzylidene)hydrazono]indolin-2-one (**3i**)* Khan *et al.* (2009).

*5-Chloro-3-[(4-nitrobenzylidene)hydrazono]indolin-2-one (**3j**)* Yield 75% (ethanol); m. p. 280°C. IR (KBr, cm^{-1}): 3316 (NH), 3073 (CH aromatic), 1686 (C=O), 1638 (C=N), 1535, 1350 (NO_2), 754 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 6.85–6.95 (m, 1H, Ar–*H*), 7.53–7.7 (m, 2H, Ar–*H*), 8.1 (d, 2H, Ar–*H*), 8.4 (d, 2H, Ar–*H*), 8.7 (s, 1H, –N=C*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 169.1, 152.0, 149.7, 142.3, 140.0, 137.9, 134.0, 132.1, 130.1, 128.6, 126.5, 124.3, 119.7. Anal. Calcd. for $C_{15}H_9ClN_4O_3$: C 54.81, H 2.76, Cl 10.79, N 17.04; Found: C 54.89, H 2.69, N 10.83%.

*5-Chloro-3-[(furan-2-ylmethylene)hydrazono]indolin-2-one (**3k**)* Yield 89% (ethanol); m. p. 265°C. IR (KBr, cm^{-1}): 3300 (NH), 3072 (CH aromatic), 1685 (C=O), 1635 (C=N), 1258 (C–O–C), 753 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 6.6 (d, 1H, Ar–*H*), 6.88–6.96 (m, 1H, Ar–*H*), 7.2 (d, 1H, Ar–*H*), 7.68–7.77 (t, 3H, Ar–*H*), 8.58 (s, 1H, –N=C*H*), 11.2 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 169.1, 163.9, 149.2, 144.2, 140.9, 137.4, 132.0, 130.0, 127.2, 123.3, 120.2, 118.1, 112.6. Anal. Calcd. for $C_{13}H_8ClN_3O_2$: C 57.05, H 2.95, N 15.35; Found: C 57.13, H 2.97, N 15.29%.

*General procedure for the synthesis of 3-(5-chloro-2-oxoindolin-3-ylideneamino)-2-arylthiazolidin-4-one (**4a–k**)*

The mixture of 5-chloro-3-[(arylidene)hydrazono] indoline-2-one (**3a–k**, 0.1 mol) and thioglycolic acid (0.1 mol) in ethanol (100 ml) in presence of anhydrous $ZnCl_2$ (a pinch) was refluxed for 10–12 h on water bath. The reaction mixture was poured into ice-cold water, filtered and finally recrystallized from appropriate solvents to give compounds **4a–k**.

*3-(5-Chloro-2-oxoindolin-3-ylidendeamino)-2-phenylthiazolidin-4-one (**4a**)* Yield 69% (methanol); m. p. 124–126°C. IR (KBr, cm^{-1}): 3310 (NH), 3070 (CH aromatic), 1771, 1680 (C=O), 1632 (C=N), 750 (C–Cl), 700 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.1 (s, 2H, CH_2 of thiazolidinone ring), 4.3 (s, 1H, –N–C*H*–Ar), 6.9–6.94 (d, 1H, Ar–*H*), 7.24–7.3 (t, 3H, Ar–*H*), 7.54–7.66 (m, 2H, Ar–*H*), 7.86–7.94 (t, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.0, 167.7, 146.2, 144.1, 141.6, 139.3, 136.7, 134.6, 132.0, 129.4, 127.1, 124.8, 118.9, 56.5, 35.6. Anal. Calcd. for $C_{17}H_{12}ClN_3O_2S$: C 57.06, H 3.38, N 11.74, S 8.96; Found: C 56.97, H 3.43, N 11.66, S 8.88%. MS: $[M]^+$ at *m*/*z* 357.81.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(2-chlorophenyl)thiazolidin-4-one (**4b**)* Yield 78% (ethanol); m. p. 188–189°C. IR (KBr, cm^{-1}): 3302 (NH), 3080 (CH aromatic), 1762, 1688 (C=O), 1627 (C=N), 750 (C–Cl), 695 (C–S-C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.22 (s, 2H, CH_2 of thiazolidinone ring), 4.8 (s, 1H, –N–C*H*–Ar), 6.9–7 (d, 1H, Ar–*H*), 7.2–7.45 (m, 5H, Ar–*H*), 8.2–8.35 (m, 1H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.3, 167.9, 150.4, 148.9, 145.5, 142.8, 140.3, 137.8, 135.2, 132.8, 130.5, 127.8, 125.6, 119.1, 102.3, 51.2, 35.9. Anal. Calcd. For $C_{17}H_{11}Cl_2N_3O_2S$: C 52.05, H 2.83, N 10.71, S 8.17; Found: C 52.11, H 2.89, N 10.66, S 8.12%. MS: $[M]^+$ at *m*/*z* 392.26.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(4-chlorophenyl)thiazolidin-4-one (**4c**)* Yield 66% (chloroform); m. p. 138–140°C. IR (KBr, cm^{-1}): 3306 (NH), 307 6 (CH aromatic), 1760, 1685 (C=O), 1624 (C=N), 745 (C–Cl), 689 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.2 (s, 2H, CH_2 of thiazolidinone ring), 4.3 (s, 1H, –N–C*H*–Ar), 6.8–7.0 (d, 1H, Ar–*H*), 7.35–7.45 (d, 2H, Ar–*H*), 7.5–7.68 (m, 2H, Ar–*H*), 7.86–7.95 (d, 2H, Ar–*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.2, 168.4, 145.1, 142.4, 140.3, 137.8, 135.6, 133.1, 130.5, 128.0, 125.7, 123.3, 119.1, 56.5, 35.1. Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O_2S$: C 52.05, H 2.83, N 10.71, S 8.17; Found: C 51.97, H 2.89, N 10.67, S 8.12%. MS: $[M]^+$ at *m*/*z* 392.26.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(3-methoxyphenyl)thiazolidin-4-one (**4d**)* Yield 74% (ethanol); m. p. 148–150°C. IR (KBr, cm^{-1}): 3315 (NH), 3074 (CH aromatic), 1764, 1682 (C=O), 1615 (C=N), 1250 (C–O–C), 748 (C–Cl), 682 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.18 (s, 2H, CH_2 of thiazolidinone ring), 3.9 (s, 3H, –OCH_3), 4.62 (s, 1H, –N–C*H*–Ar), 6.9–6.94 (d, 1H, Ar–*H*), 7.02–7.06 (d, 2H, Ar–*H*), 7.22–7.32 (m, 3H, Ar–*H*), 7.54–7.64 (m, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.2, 168.6, 160.3, 141.7, 139.5, 137.0, 134.9, 132.5, 130.2, 127.7, 125.5, 119.8, 117.1, 114.3, 112.1, 58.3, 56.2, 35.7. Anal. Calcd. for $C_{18}H_{14}ClN_3O_3S$: C 55.74, H 3.64, N 10.83, S 8.27; Found: C 55.82, H 3.57, N 10.75, S 8.18%. MS: $[M]^+$ at *m*/*z* 387.84.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(2-hydroxyphenyl)thiazolidin-4-one (**4e**)* Yield 65% (ethanol); m. p. 240–242°C. IR (KBr, cm^{-1}): 3435 (Ar–OH), 3312 (NH), 3075 (CH aromatic), 1763, 1688 (C=O), 1622 (C=N), 750 (C–Cl), 690 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.3 (s, 2H, CH_2 of thiazolidinone ring), 4.6 (s, 1H, –N–C*H*–Ar), 6.7–6.9 (d, 1H, Ar–*H*), 7.03–7.4 (m, 4H, Ar–*H*), 7.5–7.8 (m, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*), 11.4 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.4, 168.1, 153.2, 142.4, 140.0, 137.6, 135.4, 132.9, 130.6, 128.1, 125.7, 122.8, 120.4, 117.9, 115.6, 50.2, 35.6. Anal. Calcd. for $C_{17}H_{12}ClN_3O_3S$: C 54.62, H 3.24, N 11.24, S 8.58; Found: C 54.69, H 3.21, N 11.18, S 8.49%. MS: $[M]^+$ at *m*/*z* 373.81.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(4-hydroxyphenyl)thiazolidin-4-one (**4f**)* Yield 72% (ethanol); m. p. 271–272°C. IR (KBr, cm^{-1}): 3440 (Ar–OH), 3310 (NH), 3078 (CH aromatic), 1764, 1690 (C=O), 1624 (C=N), 751 (C–Cl), 689 (C–S-C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.3 (s, 2H, CH_2 of thiazolidinone ring), 4.4 (s, 1H, –N–C*H*–Ar), 6.7–6.9 (m, 3H, Ar–*H*), 7.56–7.8 (m, 4H, Ar–*H*), 10.1 (s, 1H, O*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.3, 168.5, 156.7, 141.1, 138.9, 136.7, 134.4, 131.9, 129.9, 127.6, 125.3, 119.1, 115.6, 56.9, 35.7. Anal. Calcd. for $C_{17}H_{12}ClN_3O_3S$: C 54.62, H 3.24, N 11.24, S 8.58; Found: C 54.58, H 3.16, N 11.18, S 8.47%. MS: $[M]^+$ at *m*/*z* 373.81.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-[4-(dimethylamino)phenyl]thiazolidin-4-one (**4g**)* Yield 75% (dioxan); m. p. 245–247°C. IR (KBr, cm^{-1}): 3304 (NH), 3075 (CH aromatic), 2852 (CH aliphatic), 1765, 1689 (C=O), 1616 (C=N), 749 (C–Cl), 692 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 2.4 (s, 6H, –N(CH_3)$_2$), 3.5 (s, 2H, CH_2 of thiazolidinone ring), 4.3 (s, 1H, –N–C*H*–Ar), 6.7–6.8 (d, 2H, Ar–*H*), 6.9–7.0 (d, 1H, Ar–*H*), 7.55–7.93 (m, 4H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.4, 168.8, 149.3, 142.9, 140.3, 137.8, 135.3, 132.4, 130.1, 127.5, 125.6, 119.3, 112.7, 56.2, 40.5, 35.6. Anal. Calcd. for $C_{19}H_{17}ClN_4O_2S$: C 56.93, H 4.27, N 13.98, S 8.00; Found: C 57.10, H 4.20, N 13.86, S 7.93%. MS: $[M]^+$ at *m*/*z* 400.88.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(4-methoxyphenyl)thiazolidin-4-one (**4h**)* Yield 70% (toluene); m. p. 324°C. IR (KBr, cm^{-1}): 3315 (NH), 3074 (CH aromatic), 1760, 1688 (C=O), 1627 (C=N), 1248 (C–O–C), 748 (C–Cl), 691 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.2 (s, 2H, CH_2 of thiazolidinone ring), 3.9 (s, 3H, –OCH_3), 4.6 (s, 1H, –N–C*H*–Ar), 6.68–6.73 (d, 2H, Ar–*H*), 6.9–6.94 (d, 1H, Ar–*H*), 7.44–7.64 (m, 2H, Ar–*H*), 7.83–7.88 (d, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.5, 168.6, 159.3, 145.2, 142.5, 139.4, 137.0, 133.9, 131.3, 129.2, 125.4, 119.5, 114.2, 57.5, 55.0, 35.8. Anal. Calcd. for $C_{18}H_{14}ClN_3O_3S$: C 55.74, H 3.64, N 10.83, S 8.27; Found: C 55.79, H 3.59, N 10.77%. MS: $[M]^+$ at *m*/*z* 387.84.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(4-fluorophenyl)thiazolidin-4-one (**4i**)* Yield 67% (benzene); m. p. 176–178°C. IR (KBr, cm^{-1}): 3310 (NH), 3080 (CH aromatic), 1762, 1690 (C=O), 1626 (C=N), 1150 (C–F), 750 (C–Cl), 690 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.2 (s, 2H, CH_2 of thiazolidinone ring), 4.6 (s, 1H, –N–C*H*–Ar), 6.8–7.0 (d, 1H, Ar–*H*), 7.25–7.38 (d, 2H, Ar–*H*), 7.49–7.7 (m, 2H, Ar–*H*), 7.85–7.98 (m, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.1, 168.7, 161.3, 141.5, 139.2, 136.8, 134.4, 132.3, 129.9, 127.5, 125.2, 119.4, 115.2, 56.3, 36.1. Anal. Calcd. for $C_{17}H_{11}ClFN_3O_2S$: C 54.33, H 2.95, N 11.18, S 8.53; Found: C 54.41, H 3.10, N 11.09, S 8.45%. MS: $[M]^+$ at *m*/*z* 374.5.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(4-nitrophenyl)thiazolidin-4-one (**4j**)* Yield 57% (benzene); m.

p. 196–198°C. IR (KBr, cm^{-1}): 3310 (NH), 3075 (CH aromatic), 1762, 1685 (C=O), 1627 (C=N), 1540, 1346 (NO_2), 748 (C–Cl), 690 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.2 (s, 2H, CH_2 of thiazolidinone ring), 4.4 (s, 1H, –N–C*H*–Ar), 6.8–7.0 (m, 1H, Ar–*H*), 7.5–7.7 (m, 2H, Ar–*H*), 8.0–8.25 (d, 2H, Ar–*H*), 8.75–8.92 (d, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 170.7, 168.3, 147.6, 145.3, 139.4, 137.1, 134.9, 132.6, 130.4, 128.3, 126.0, 123.6, 119.1, 56.7, 35.8. Anal. Calcd. for $C_{17}H_{11}ClN_4O_4S$: C 50.69, H 2.75, N 13.91, S 7.96; Found: C 50.74, H 2.67, N 13.83, S 7.89%. MS: $[M]^+$ at *m/z* 402.81.

*3-(5-Chloro-2-oxoindolin-3-ylideneamino)-2-(furan-2-yl) thiazolidin-4-one (**4k**)* Yield 63% (methanol); m. p. 310°C. IR (KBr, cm^{-1}): 3308 (NH), 3080 (CH aromatic), 1760, 1690 (C=O), 1624 (C=N), 1250 (C–O–C), 750 (C–Cl), 692 (C–S–C); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.3 (s, 2H, CH_2 of thiazolidinone ring), 4.52 (s, 1H, –N–C*H*–Ar), 6.5–6.7 (d, 1H, Ar–*H*), 6.85–6.98 (m, 1H, Ar–*H*), 7.15–7.28 (d, 1H, Ar–*H*), 7.68–7.78 (t, 3H, Ar–*H*), 11.2 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 171.4, 168.9, 151.5, 141.7, 139.3, 136.9, 134.4, 131.9, 129.6, 125.5, 119.5, 109.6, 107.2, 55.8, 33.6. Anal. Calcd. for $C_{15}H_{10}ClN_3O_3S$: C 51.80, H 2.90, N 12.08, S 9.22; Found: C 51.91, H 2.96, N 11.98, S 9.12%. MS: $[M]^+$ at *m/z* 347.78.

*General procedure for the preparation of 5-chloro-3-(3-chloro-2-oxo-4-arylazetidin-1-ylimino)indolin-2-one (**5a**–**k**)*

To a stirred solution of 5-chloro-3-[(arylidene)hydrazono] indoline-2-one (**3a**–**k**, 0.1 mol) in dioxan (100 ml), chloroacetylchloride (0.1 mol) was added dropwise at 0–5°C temperature in presence of triethylamine. The reaction mixture was stirred for about 8 h and the precipitate of amine hydrochloride was filtered off. The excess of dioxan was distilled off. The mass thus obtained was cooled, poured in ice-cold water, filtered, washed, dried and recrystallized from appropriate solvents to furnish compounds **5a**–**k**.

*5-Chloro-3-(3-chloro-2-oxo-4-pheylazetidin-1-ylimino)indolin-2-one (**5a**)* Yield 85% (ethanol); m. p. 140–142°C. IR (KBr, cm^{-1}): 3315 (NH), 3080 (CH aromatic), 1745, 1720 (C=O), 1625 (C=N), 740 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.6 (s, 1H, C*H*Cl), 5.2 (s, 1H, –N–C*H*Ar), 6.9–6.94 (d, 1H, Ar–*H*), 7.18–7.24 (t, 3H, Ar–*H*), 7.4–7.5 (m, 2H, Ar–*H*), 7.8–7.86 (t, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 169.3, 166.5, 144.1, 140.0, 138.0, 136.1, 134.2, 132.4, 130.6, 128.9, 127.1, 125.3, 119.6, 64.5, 61.4. Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O_2$: C 56.69, H 3.08, N 11.67; Found: C 56.77, H 2.98, N 11.58%. MS: $[M]^+$ at *m/z* 359.00.

*5-Chloro-3-[3-chloro-2-(2-chlorophenyl)-4-oxazetidin-1-ylimino]indolin-2-one (**5b**)* Yield 76% (ethanol); m. p. 120°C. IR (KBr, cm^{-1}): 3312 (NH), 3078 (CH aromatic), 1760, 1728 (C=O), 1622 (C=N), 744 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.25 (s, 1H, C*H*Cl), 5.2 (s, 1H, –N–C*H*Ar), 6.8–7.0 (d, 1H, Ar–*H*), 7.15–7.4 (m, 5H, Ar–*H*), 7.95–8.05 (m, 1H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.2, 165.5, 146.2, 144.7, 142.5, 140.9, 139.0, 136,8, 135.1, 133.0, 131.4, 129.5, 127.2, 125.3, 119.1, 63.8, 56.2. Anal. Calcd. for $C_{17}H_{10}Cl_3N_3O_2$: C 51.74, H 2.55, N 10.65; Found: C 51.81, H 2.59, N 10.74%. MS: $[M]^+$ at *m/z* 392.98.

*5-Chloro-3-[3-chloro-2-(4-chlorophenyl)-4-oxoazetidin-1-ylimino]indolin-2-one (**5c**)* Yield 82% (ethanol); m. p. 170–172°C. IR (KBr, cm^{-1}): 3309 (NH), 3075 (CH aromatic), 1750, 1720 (C=O), 1626 (C=N), 750 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.38 (s, 1H, C*H*Cl), 5.4 (s, 1H, –N–C*H*Ar), 6.9–7.0 (d, 1H, Ar–*H*), 7.2–7.3 (d, 2H, Ar–*H*), 7.35–7.5 (m, 2H, Ar–*H*), 7.7–7.8 (d, 2H, Ar–*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.0, 166.2, 142.3, 140.4, 138.0, 136.3, 134.4, 132.2, 130.2, 128.1, 126.2, 124.2, 119.1, 64.5, 61.3. Anal. Calcd. For $C_{17}H_{10}Cl_3N_3O_2$: C 51.74, H 2.55, N 10.65; Found: C 51.83, H 2.48, N 10.57%. MS: $[M]^+$ at *m/z* 392.98.

*5-Chloro-3-[3-chloro-2-(3-methoxyphenyl)-4-oxoazetidin-1-ylimino]indolin-2-one (**5d**)* Yield 80% (ethanol); m. p. 138°C. IR (KBr, cm^{-1}): 3312 (NH), 3078 (CH aromatic), 1753, 1721 (C=O), 1618 (C=N), 1252 (C–O–C), 749 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.9 (s, 3H, –OCH_3), 4.8 (s, 1H, C*H*Cl), 5.2 (s, 1H, –N–C*H*Ar), 6.98–7.2 (d, 1H, Ar–*H*), 7.1–7.14 (d, 1H, Ar–*H*), 7.3–7.4 (m, 3H, Ar–*H*), 7.62–7.72 (m, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.7, 166.5, 160.6, 144.7, 139.3, 134.2, 132.3, 130.2, 128.6, 126.8, 124.9, 121.1, 119.2, 113.9, 112.0, 64.5, 61.7, 55.6. Anal. Calcd. for $C_{18}H_{13}Cl_2N_3O_3$: C 55.40, H 3.36, N 10.77; Found: C 55.49, H 3.31, N 10.68%. MS: $[M]^+$ at *m/z* 390.22.

*5-Chloro-3-[3-chloro-2-(2-hydroxyphenyl)-4-oxoazetidin-1-ylimino]indolin-2-one (**5e**)* Yield 75% (dioxan); m. p. 109°C. IR (KBr, cm^{-1}): 3430 (Ar–OH), 3310 (NH), 3075 (CH aromatic), 1748, 1726 (C=O), 1624 (C=N), 746 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.8 (s, 1H, C*H*Cl), 5.5 (s, 1H, –N–C*H*Ar), 6.96–7.2 (d, 1H, Ar–*H*), 7.22–7.3 (m, 4H, Ar–*H*), 7.62–7.72 (m, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*), 11.5 (s, 1H, O*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.0, 166.1, 154.2, 140.8, 138.4, 136.5, 134.6, 132.7,

130.9, 129.0, 127.1, 125.2, 121.2, 119.3, 115.5, 64.8, 55.2. Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O_3$: C 54.28, H 2.95, N 11.17; Found: C 54.36, H 3.10, N 11.06%. MS: $[M]^+$ at *m/z* 376.19.

5-Chloro-3-[3-chloro-2-(4-hydroxyphenyl)-4-oxoazetidin-1-ylimino]indolin-2-one ***(5f)*** Yield 84% (chloroform); m. p. 160–162°C. IR (KBr, cm^{-1}): 3438 (Ar–OH), 3315 (NH), 3080 (CH aromatic), 1759, 1720 (C=O), 1620 (C=N), 752 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.8 (s, 1H, C*H*Cl), 5.4 (s, 1H, –N–C*H*Ar), 6.98–7.1 (d, 1H, Ar–*H*), 7.1–7.2 (d, 2H, Ar–*H*), 7.4–7.65 (m, 4H, Ar–*H*), 10.1 (s, 1H, O*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.3, 166.0, 156.7, 139.4, 135.2, 133.2, 131.3, 129.9, 128.3, 126.7, 125.1, 119.2, 115.8, 64.6, 61.2. Anal. Calcd. for $C_{17}H_{11}Cl_2N_3O_3$: C 54.28, H 2.95, N 11.17; Found: C 54.36, H 3.04, N 11.09%. MS: $[M]^+$ at *m/z* 376.19.

5-Chloro-3-[3-chloro-2-{4-(dimethylamino)phenyl}-4-oxoazetidin-1-ylimino]indolin-2-one ***(5g)*** Yield 78% (ethylacetate); m. p. 149–150°C. IR (KBr, cm^{-1}): 3308 (NH), 3082 (CH aromatic), 2860 (CH aliphatic), 1750, 1722 (C=O), 1620 (C=N), 748 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 2.4 (s, 6H, –N(CH_3)$_2$), 4.8 (s, 1H, C*H*Cl), 5.3 (s, 1H, –N–C*H*Ar), 6.75–6.85 (d, 2H, Ar–*H*), 6.9–7.1 (d, 1H, Ar–*H*), 7.7–8.0 (m, 4H, Ar–*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.8, 166.3, 149.2, 139.0, 136.0, 133.7, 131.8, 129.5, 127.2, 125.1, 119.3, 112.4, 64.1, 61.6, 40.5. Anal. Calcd. for $C_{19}H_{16}Cl_2N_4O_2$: C 56.59, H 4.00, N 13.89; Found: C 56.66, H 3.95, N 13.81%. MS: $[M]^+$ at *m/z* 403.26.

5-Chloro-3-[3-chloro-2-(4-methoxyphenyl)-4-oxoazetidin-1-ylimino]indolin-2-one ***(5h)*** Yield 87% (ethanol); m. p. 112°C. IR (KBr, cm^{-1}): 3310 (NH), 3080 (CH aromatic), 1747, 1721 (C=O), 1625 (C=N), 1250 (C–O–C), 750 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 3.85 (s, 3H, –OCH_3), 4.6 (s, 1H, C*H*Cl), 5.42 (s, 1H, –N–C*H*Ar), 6.68–6.74 (d, 2H, Ar–*H*), 6.9–6.94 (d, 1H, Ar–*H*), 7.38–7.48 (m, 2H, Ar–*H*), 7.66–7.72 (d, 2H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.0, 166.1, 158.4, 139.5, 136.6, 134.7, 133.0, 131.1, 129.1, 127.2, 125.3, 119.5, 114.0, 64.8, 61.4, 55.5. Anal. Calcd. for $C_{18}H_{13}Cl_2N_3O_3$: C 55.40, H 3.36, N 10.77; Found: C 55.49, H 3.42, N 10.69%. MS: $[M]^+$ at *m/z* 390.22.

5-Chloro-3-[3-chloro-2-(4-fluorophenyl)-4-oxoazetidin-1-ylimino]indolin-2-one ***(5i)*** Yield 76% (benzene); m. p. 154°C. IR (KBr, cm^{-1}): 3313 (NH), 3078 (CH aromatic), 1752, 1720 (C=O), 1620 (C=N), 1140 (C–F), 740 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.78 (s, 1H, C*H*Cl), 5.19 (s, 1H, –N–C*H*Ar), 6.95–7.05 (d, 1H, Ar–*H*), 7.25–7.35 (t, 2H, Ar–*H*), 7.5–7.7 (m, 2H, Ar–*H*), 7.85–7.95 (m, 2H, Ar–*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.4, 166.1, 161.0, 141.4, 139.3, 133.9, 132.0, 130.1, 128.0, 126.3, 124.2, 119.1, 115.5, 64.4, 61.2. Anal. Calcd. for $C_{17}H_{10}Cl_2FN_3O_2$: C 53.99, H 2.67, N 11.11; Found: C 54.08, H 2.59, N 11.04%. MS: $[M]^+$ at *m/z* 378.18.

5-Chloro-3-[3-chloro-2-(4-nitrophenyl)-4-oxoazetidin-1-ylimino]indolin-2-one ***(5j)*** Yield 81% (toluene); m. p. 212°C. IR (KBr, cm^{-1}): 3315 (NH), 3082 (CH aromatic), 1759, 1728 (C=O), 1625 (C=N), 1544, 1348 (NO_2), 742 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.9 (s, 1H, C*H*Cl), 5.19 (s, 1H, –N–C*H*Ar), 6.95–7.08 (m, 1H, Ar–*H*), 7.65–7.8 (m, 2H, Ar–*H*), 8.05–8.15 (d, 2H, Ar–*H*), 8.35–8.5 (d, 2H, Ar–*H*), 11.0 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.2, 166.1, 149.6, 145.8, 139.5, 133.7, 131.6, 129.5, 127.6, 125.5, 123.5, 121.7, 119.2, 64.0, 61.5. Anal. Calcd. for $C_{17}H_{10}Cl_2N_4O_4$: C 50.39, H 2.49, N 13.83; Found: C 50.48, H 2.41, N 13.74%. MS: $[M]^+$ at *m/z* 405.19.

5-Chloro-3-[3-chloro-2-(furan-2-yl)-4-oxoazetidin-1-ylimino]indolin-2-one ***(5k)*** Yield 85% (methanol); m. p. 102°C. IR (KBr, cm^{-1}): 3312 (NH), 3080 (CH aromatic), 1760, 1725 (C=O), 1620 (C=N), 1253 (C–O–C), 746 (C–Cl); ^{1}H NMR (DMSO-d_6) δ in ppm: 4.7 (s, 1H, C*H*Cl), 5.18 (s, 1H, –N–C*H*Ar), 6.7–6.9 (d, 1H, Ar–*H*), 6.95–7.1 (m, 1H, Ar–*H*), 7.25–7.4 (d, 1H, Ar–*H*), 7.75–7.9 (t, 3H, Ar–*H*), 11.1 (s, 1H, Het-N*H*); ^{13}C NMR (DMSO-d_6) δ in ppm: 168.4, 166.3, 151.1, 141.6, 139.5, 134.7, 132.6, 130.8, 128.9, 125.2, 119.1, 111.3, 109.1, 62.2, 59.3. Anal. Calcd. for $C_{15}H_9Cl_2N_3O_3$: C 51.45, H 2.59, N 12.00; Found: C 51.56, H 2.48, N 11.94%. MS: $[M]^+$ at *m/z* 350.16.

Antibacterial and antifungal activity (MIC)

The bacterial and fungal strains were procured from National Chemical Laboratory (NCL), Pune, India. The antibacterial activity of the synthesized compounds was screened against the following bacterial strains: *Bacillus subtilis* ATCC 6633, *Staphylococcus epidermidis* ATCC 12228, *Micrococcus luteus* ATCC 4698, *Staphylococcus aureus* ATCC 25923, *Staphylococcus hominis* ATCC 27844, *Bacillus pumilus* ATCC 14884, *Bacillus cereus* ATCC 11778, *Proteus vulgaris* ATCC 13315, *Proteus mirabilis* ATCC 49565, *Salmonella typhi* ATCC 19430, *Klebsiella pneumonia* ATCC 13883, *Escherichia coli* ATCC 25922 and *Pseudomonas aeroginosa* ATCC 10145.

The compounds were also screened against the following fungal strains: *Aspergillus niger* ATCC 9142,

Aspergillus awamori ATCC 22342, *Candida albicans* ATCC 10231, *Alternaria alternate* ATCC 66868, *Microsporum canis* ATCC 11622, *Rhizoctonia solani* ATCC 76131, *Trichophyton longiformis* ATCC 22397, *Aspergillus flavus* ATCC 15517, *Fusarium solani* ATCC 38136 and *Trichoderma viride* ATCC 52440.

The MIC was done by broth dilution method. Nutrient broth and potato dextrose broth was procured from Himedia Laboratories. A set of sterilized test tubes with nutrient broth medium capped with cotton plugs were taken (1–12). The test compounds were dissolved in suitable solvent (DMF) and at the concentration of 600 μg ml^{-1}, which were serially diluted from 1 to 12. A fixed volume of 0.5 ml culture was added in all the test tubes and was incubated at 37°C for 24 h. After 24 h, tubes were observed visually for turbidity.

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