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**Research Article**

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# Synthesis, characterization and biological evaluation of multi substituted quinoline-thiazolidinone mannich bases

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**ABSTRACT**

*A series of total six novel Quinoline Schiff bases were prepared from 5-amino-8-hydroxy quinoline and substituted aldehydes. All quinoline schiff bases were refluxed with thioacetic acid in presence of anhydrous zinc chloride and solvent N,N-dimethyl formamide to afforded novel series of 4-thiazolidinone [1a-f]. Novel Mannich bases (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl) oxy)acetohydrazide were synthesized by the condensation of 2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide with Isatin afford corresponding (Z)-2-((5-(4-oxo-2-(4-substituted phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene) acetohydrazide. This was subjected to mannich reaction with cyclic secondary amines such as piperidine / morpholine / N-Methyl Piperazine in presence of formaldehyde in DMF to give corresponding Mannich bases bases (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl)oxy) acetohydrazide in excellent yields. The structures of these newly synthesized compounds were characterized by $^{1}$H-NMR, $^{13}$C-NMR, Mass, IR and elemental analysis. The prepared compounds have been screened on some stains of bacteria and fungai.*

**Keywords:** Thiazolidinones, quinoline, Mannich bases, Anti-microbial activity

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## INTRODUCTION

Thiazolidinone, a saturated form of thiazole with carbonyl group on fourth carbon posses almost all types of biological activities. This diversity in the biological response profile has attracted the attention of many researchers to explore this skeleton to its multiple potential against several activities. Among pharmacologically important heterocyclic compounds, 4-thiazolidinone derivatives have been known to possess a wide range of biological properties such as antimicrobial[1-7,25-28] anticonvulsant [9], anti-HIV [10], antifungal [11], antibacterial agents[12], anti-inflammatory, analgesic[2] cytotoxic[8]. 8-hydroxy quninolines constitute another class of heterocyclics. A series of compounds derived from 8-hydroxy quninolines were recently synthesised as potential HIV-1 integrase inhibitors [13-16]. Some new 8-hydroxy quinolines also possess interesting herbicidal, antimicrobial activities [17-23]. Mannich bases of azetidinones containing quinoline derivatives plays pivotal role in medicinal chemistry.

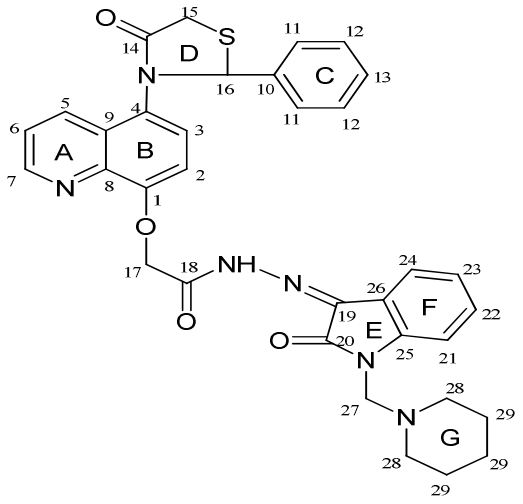
The area in which mannich bases of thiazolidinone-quinoline derivatives have not reported so far. Hence it was thought worthwhile to synthesise some new congeners thiazolidinone heterocyclics by incorporating the 8-hydroxy quinoline and thiazolidin-4-one moieties in a single molecular frame work. The present work deals with the synthesis of the title compounds using the synthon 5-amino-8-hydroxy quinoline followed by their antimicrobial screening.

## EXPERIMENTAL SECTION

Melting points were determined on open capillaries using a cintex melting point apparatus. T.L.C analyses were performed on precoated silicagel (E-Merck Kieselgel $60F_{254}$) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. Column chromatography was conducted by using silica gel with different solvent systems as elutes. IR Spectra were recorded in KBr on Perkin-Elmer Spectrum BX series FT-IR spectrometer. $^1$H-NMR spectrum were recorded on Varian Gemini 300MHz spectrometers using TMS as internal standard (chemical shifts in δ ppm). 13C-NMR Spectra were recorded on a Brucker 75MHz spectrometer. Mass spectra were scanned on a varian MATCH-7 and Jeol JMSD-300 mass spectrometer at 70ev. Elemental analyses were carried out on a carloerba 106 and Perkin-Elmer Analyser. All the chemicals used in the present investigation were purchased from Aldrich chemicals; U.S.A. 5-Amino-8-Hydroxy quinoline was prepared by a reported method [24]

## RESULTS AND DISCUSSION

5-Amino-8-Hydroxy quinolone on condensation with 4-substituted benzaldehydes yielded 5-(benzylideneamino)quinolin-8-ol (C). Compound-C on treatment with Thioaceticacid afford a 3-(8-hydroxyquinolin-5-yl)-2-(4-substitutedphenyl)thiazolidin-4-one (1) with yield of 58%. Compound (1) on reaction with chlroethyl acetate yielded compound-2 with 50% yield. Compound-2 on amination with hydrazine hydrate afford a 2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3a- f). The condensation reaction of compound-3 with isatin (4) yielded (Z)-2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)acetohydrazide (5af). Compounds (5a-f) on reaction with formaldehyde and piperidine / morpholine / N-methyl piperazine afford compounds 6a-f. These reactions are summarised in the scheme-I. Yields were moderate to fair (40-70%). The purity of the compounds was monitored by TLC.




In IR spectra compounds 6a-f showed broad band around 3190 $cm^{-1}$, strong bands in the region of 3040, 1613, 1698, 1710 $cm^{-1}$ and a weak band at 1188 $cm^{-1}$ indicating the presence of characteristic peaks for –NH, Ar-H str, -C=N, thiazolidinone –C=O, amide –CONH and –C-S groups respectively. In $^1$H-NMR ($(CD)_2SO$) the compounds (6a) shown δ: 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, $–CH_2–N–CH_2$ of piperidine ring), 4.6(s,2H,N-$CH_2$-N), 4.8(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.26-7.81(m, 9H $C_6H_5$ of phenyl, $C_6H_4$ of indole), 8.1-8.8 (m,5H of quinoline ring), 9.52(s, 1H, -NH). The $^{13}$C-NMR spectrum of ($CDCl_3$) shown δ: 150-$C_1$, 107-$C_2$, 116-$C_3$, 134-$C_4$, 129-$C_5$, 121-$C_6$, 149-$C_7$, 141-$C_8$, 122-$C_9$ (quinoline ring A&B), 139-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$ ( thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 130-$C_{24}$,147-$C_{25}$, 117-$C_{26}$ (indole ring E&F), 75-$C_{27}$, 55-$C_{28}$, 26-$C_{29}$ (Piperidine ring G). Mass spectrum of 6a was recorded by ESI-MS technique showed the molecular ion signal at 620.22. The spectral values are in good agreement with the structure of the compound (6a)

### 3.1. Anti- Bacterial Activity

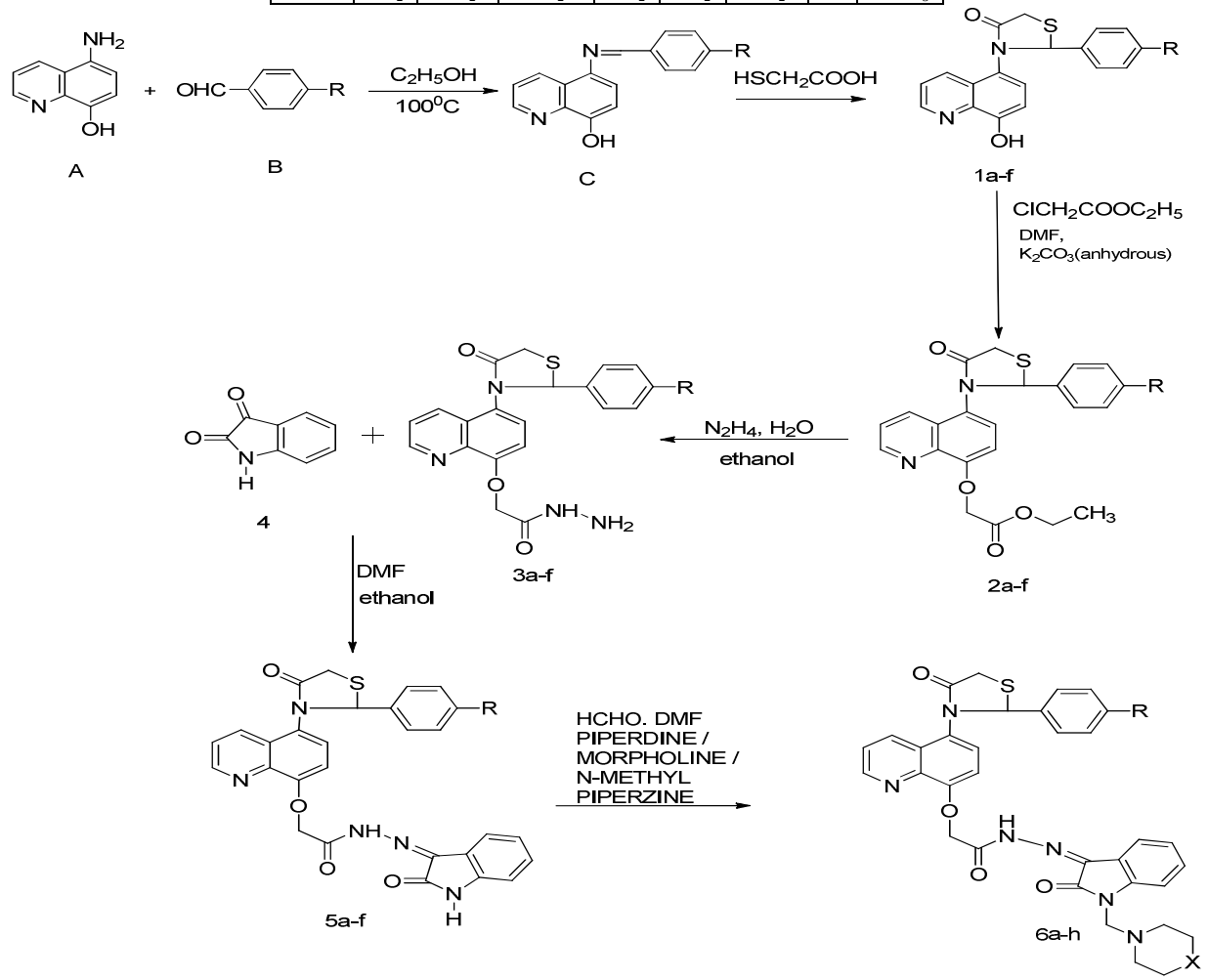
The anti-bacterial activity of 6a-h was determined by the disc diffusion method with Cefaclor (100µg/ml) as the reference antibiotics [29]. The newly synthesised compounds were examined, respectively against *Staphylococcus*

*aureus, Bacillus cereus, Escherichia c-oli* and *Pseudomonas aeruginosa* bacteria. The test results presented in the table-2, suggest that –Nitro, -Chloro, –Bromo and morpholine derivatives exhibit high activity against the tested bacteria, the rest of the compounds were found to be either slightly active or inactive against the tested microorganisms.

### 3.2. Antifungal Activity

The antifungal activity of 6a-h were tested against two different fungi such as *Asperigillus flavus* and *Candida albicans* by disc diffusion method [29] with Clotrimazole as standard(100µg/ml). The test results presented in the table-3, suggest that –Nitro, -Chloro, –Bromo and morpholine derivatives exhibit high activity against the fungi species tested, the rest of the compounds were found to be either slightly active or inactive against the fungi species tested.

| Comp | 6a | 6b | 6c | 6d | 6e | 6f | 6g | 6h |
|---|---|---|---|---|---|---|---|---|
| R | H | 4-$CH_3$ | 4-$OCH_3$ | 4-Cl | 4-Br | 4-$NO_2$ | H | H |
| X | $CH_2$ | $CH_2$ | $CH_2$ | $CH_2$ | $CH_2$ | $CH_2$ | O | N-$CH_3$ |




**Scheme-I**

### 3.3. Synthesis of 3-(8-hydroxyquinolin-5-yl)-2-(4-substitutedphenyl)thiazolidin-4-one (1a-f)

Equimolar quantity of 5-Amino-8-hydroxyquinoline and 4-substituted benzaldehydes were dissolved in absolute alcohol, to this three drops of acetic acid is added then heated on a steam bath for 5-6h at 100°C. After standing for 24h at room temperature, the product was dried and recrystallized from warm absolute alcohol.

A mixture of schiff's base (0.0 mol) and mercaptoacetic acid (0.01 mol) dissolved in diaoxane (20 ml), anhydrous zinc chloride (0.5 mg) was added and refluxed for 8 hrs. The reaction was cooled and the resulting solid was washed with sodium bicarbonate solution and recrystalised from absolute alcohol. The structure of 1a was established by spectral analysis.

**IR(KBr):** 3340cm$^{-1}$, 1690 cm$^{-1}$ and 1156 cm$^{-1}$ due to stretching vibrations of –OH, >C=O, C-O / bending vibrations of –OH respectively. **$^1$H-NMR(300MHz, (CD)$_2$SO, TMS) Spectra:** δ=4.6(s,1H,-OH), 6.44(s,1H,-CH of thiazolidinone attached to phenyl ring), 3.85(s,2H,-$CH_2$ of thiazolidinone), 7.25-7.36(m, 5H of $C_6H_5$), 7.6-8.8(m,5H of quinolinne ring).

**3.4. Ethyl-2-(5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yloxy)acetate (2a-f)**

A mixture of 3-(8-hydroxyquinolin-5-yl)-2-p-tolylthiazolidin-4-one (1a) (0.02M) anhydrous $K_2CO_3$ (0.03M), chloro ethyl acetate (0.02M) and DMF was stirred at room temperature for 8 hours, the reaction mixture was diluted with ice-cold water. The separated solid was identified as (2a). This was collected by filtration and recrystallized from ethanol.

**3.5. Synthesis of 2-(5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yloxy) acetohydrazide (3a-f)**

A solution of **(2a)** (0.01M) and hydrazine hydrate (0.015M) in ethanol 20 mL was refluxed for 5 hours. The reaction mixture was cooled and poured on to ice cold water with stirring. The separated solid was filtered, washed with water and recrystallized from ethanol to afford **(3a**). Other compounds of the series were similarly prepared (3b-f).

**3.5.1.2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3a)**

IR(KBr): 1620(-C=N), 1698(-C=O), 3200(-NH), 3498,3416(-$NH_2$), 3040(Ar-H), 1188cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.05(s,2H,-$NH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.58(s,2H,-O-$CH_2$), 7.25-7.36(m, 5H of $C_6H_5$), 7.6-8.8(m,5H of quinolinne ring), 9.52(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 146-$C_1$, 107-$C_2$, 117-$C_3$, 134-$C_4$, 128-$C_5$, 121-$C_6$, 149-$C_7$, 141-$C_8$, 122-$C_9$ (quinoline ring A&B), 139-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 32-$C_{15}$, 73-$C_{16}$ (thiazolidinone ring D), 67-$C_{17}$(O-$CH_2$).

**3.5.2.2-((5-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3b)**

IR(KBr): 1618(-C=N), 1696(-C=O), 3206(-NH), 3498,3412(-$NH_2$), 3040(Ar-H), 1149cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.10(s,2H,-$NH_2$), 3.10(s,3H,Ar-$CH_3$), 6.38(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.80(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.55(s,2H,-O-$CH_2$), 7.1-7.2(m, 4H of $C_6H_4$), 7.68-8.84(m,5H of quinolinne ring), 9.56(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 145-$C_1$, 107-$C_2$, 118-$C_3$, 133-$C_4$, 129-$C_5$, 120-$C_6$, 148-$C_7$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 141--$C_{10}$, 127--$C_{11}$, 129-$C_{12}$, 136-$C_{13}$ (phenyl ring C), 169-$C_{14\&18}$, 35-$C_{15}$, 73-$C_{16}$ (thiazolidinone ring D), 68-$C_{17}$(O-$CH_2$), 21(Ar-$CH_3$).

**3.5.3.2-((5-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy) acetohydrazide (3c)**

IR(KBr): 1621(-C=N), 1692(-C=O), 3208(-NH), 3496,3412(-$NH_2$), 3040(Ar-H), 1156cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.12(s,2H,-$NH_2$), 3.8(s,3H,-O-$CH_3$), 6.42(s,1H,-CH of Thiazolidin attached to phenyl ring), 4.0(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.63(s,2H,-O-$CH_2$), 7.1-7.6(m, 4H of $C_6H_4$), 7.8-8.8(m,5H of quinolinne ring), 9.58(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 149-$C_1$, 108-$C_2$, 117-$C_3$, 133-$C_4$, 129-$C_5$, 122-$C_6$, 149-$C_7$, 140-$C_8$, 122-$C_9$(quinoline ring A&B), 136-$C_{10}$, 128-$C_{11}$, 113-$C_{12}$, 158-$C_{13}$ (phenyl ring C), 172-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$ (thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 55.9(O-$CH_3$).

**3.5.4.2-((5-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3d)**

IR(KBr): 1617(-C=N), 1680(-C=O), 3210(-NH), 3495,3413(-$NH_2$), 3042(Ar-H), 1185cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.14(s,2H,-$NH_2$), 6.38(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.92(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.56(s,2H,-O-$CH_2$), 7.1-7.4(m, 4H of $C_6H_4$), 7.7-8.7(m,5H of quinolinne ring), 9.58(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 150-$C_1$, 107-$C_2$, 117-$C_3$, 135-$C_4$, 128-$C_5$, 123-$C_6$, 148-$C_7$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 141-$C_{10}$, 128-$C_{11}$, 133-$C_{12}$, 121-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 72-$C_{16}$, 69-$C_{17}$(O-$CH_2$).

**3.5.5.2-((5-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3e)**

IR(KBr): 1620(-C=N), 1698(-C=O), 3209(-NH), 3498,3414(-$NH_2$), 3040(Ar-H), 1138cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.14(s,2H,-$NH_2$), 6.46(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.95(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.56(s,2H,-O-$CH_2$), 7.1-7.8(m, 4H of $C_6H_4$), 7.7-8.9(m,5H of quinolinne ring), 9.54(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 148-$C_1$, 107-$C_2$, 117-$C_3$, 133-$C_4$, 128-$C_5$, 123-$C_6$, 148-$C_7$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 143-$C_{10}$, 130-$C_{11}$, 132-$C_{12}$, 121-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 32-$C_{15}$, 74-$C_{16}$(thiazolidinone ring D), 68(O-$CH_2$).

**3.5.6.2-((5-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (3f)**

IR(KBr): 1615(-C=N), 1696(-C=O), 3210(-NH), 3498,3415(-$NH_2$), 3040(Ar-H), 1149cm$^{-1}$ (C-S). $^1$HNMR(300MHZ, (CD)$_2$SO, TMS): δ= 2.12(s,2H,-$NH_2$), 6.42(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 4.65(s,2H,-O-$CH_2$), 7.1-8.4(m, 9H, $C_6H_4$ of phenyl, $C_9H_5N$ of

quinoline), 9.57(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 149-$C_1$, 108-$C_2$, 118-$C_3$, 134-$C_4$, 128-$C_5$, 123-$C_6$,149-$C_7$, 140-$C_8$,123-$C_9$(quinoline ring A&B), 150-$C_{10}$, 128-$C_{11}$, 122-$C_{12}$, 146-$C_{13}$ (phenyl ring C), 171-$C_{1418}$, 33-$C_{15}$, 75-$C_{16}$(thiazolidinone ring D), 70-$C_{17}$(O-$CH_2$).

**3.6. Synthesis of (Z)-2-((5-(4-oxo-2-(4-substitutedphenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)acetohydrazide (5a-f)**

Equimolar quantities (0.01 mol) of Isatin **(4)** and the corresponding amino compound **(3a-f)** were dissolved in warm ethanol (40 mL) containing DMF (0.5 mL). The reaction mixture was refluxed for 1-4 hours and then kept at room temperature overnight. The resulting solid was filtered and washed with ethanol, dried and recrystallized from ethanol to afford compounds **(5a-f)**.

**3.6.1.(Z)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)acetohydrazide (5a)**

IR(KBr): 1617(-C=N), 1188(C-S), 1705(NH-C=O), 1692(Thiazolidinone-C=O), 3226 (-NH), 3040cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 4.8(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.26-7.61(m, 9H of $C_6H_5$, $C_6H_4$ of indole), 7.72-8.8 (m,5H of quinoline ring), 9.74(s, 1H, -NH), 10.10(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 149-$C_1$, 107-$C_2$, 116-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$, 147-$C_{7\&25}$, 141-$C_8$, 122-$C_9$(quinoline ring A&B), 139-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 135-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 129-$C_{24}$, 117-$C_{26}$(Indole ring E&F).

**3.6.2.(Z)-2-((5-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)acetohydrazide (5b)**

IR(KBr): 1620(-C=N), 1179(C-S), 1696(NH-C=O), 1698(Thiazolidinone-C=O), 3225 (-NH), 3041cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 3.10 (s, 3H, Ar-$CH_3$), 4.74(s,2H,-O-$CH_2$), 6.42(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.81(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.20-7.70 (m, 8H $C_6H_4$ phenyl, $C_6H_4$ of indole), 7.95-8.81 (m,5H of quinoline ring), 9.72(s, 1H, -NH), 10.16(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 148-$C_1$, 107-$C_2$, 116-$C_3$, 133-$C_4$, 129-$C_5$, 120-$C_6$, 148-$C_{7\&25}$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 141-$C_{10}$, 127-$C_{11}$, 129-$C_{12}$, 136-$C_{13}$(phenyl ring C), 169-$C_{14\&18}$, 35-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 134-$C_{19}$, 163-$C_{20}$, 122-$C_{21}$, 132-$C_{22}$, 125-$C_{23}$, 129-$C_{24}$, 117-$C_{26}$(Indole ring E&F), 25(Ar-$CH_3$).

**3.6.3.(Z)-2-((5-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)aceto -hydrazide (5c)**

IR(KBr): 1615(-C=N), 1166(C-S), 1695(NH-C=O), 1696(Thiazolidinone-C=O), 3226 (-NH), 3040cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 3.8 (s, 3H, O-$CH_3$), 4.72(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.78(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.1-7.8 (m, 8H of $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.90-8.82 (m,5H of quinoline ring), 9.69(s, 1H, -NH), 10.16(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 149-$C_1$, 108-$C_2$, 116-$C_3$, 133-$C_4$, 129-$C_5$, 121-$C_6$, 146-$C_{7\&25}$, 140-$C_8$, 122-$C_9$(quinoline ring A&B), 136-$C_{10}$, 128-$C_{11}$, 114-$C_{12}$, 158-$C_{13}$ (phenyl ring C), 172-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 135-$C_{19}$, 162-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$, 118-$C_{26}$(Indole ring E&F), 56(Ar-O-$CH_3$).

**3.6.4.(Z)-2-((5-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)aceto -hydrazide (5d)**

IR(KBr): 1620(-C=N), 1185(C-S), 1698(NH-C=O), 1692(Thiazolidinone-C=O), 3126 (-NH), 3042cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 4.68(s,2H,-O-$CH_2$), 6.38(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.92(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.0-7.8 (m, 8H of $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.95-8.84 (m,5H of quinoline ring), 9.74(s, 1H, -NH), 10.20(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 150-$C_1$, 107-$C_2$, 117-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$, 148-$C_{7\&25}$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 141-$C_{10}$, 128-$C_{11}$, 132-$C_{12}$, 121-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 72-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 135-$C_{19}$, 163-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$, 118-$C_{26}$(Indole ring E&F).

**3.6.5. (Z)-2-((5-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)aceto -hydrazide (5e)**

IR(KBr): 1617(-C=N), 1178(C-S), 1703(NH-C=O), 1692(Thiazolidinone-C=O), 3126 (-NH), 3040cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 4.72(s,2H,-O-$CH_2$), 6.48(s,1H,-CH of Thiazolidin attached to phenyl ring), 4.1(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.05-7.78 (m, 8H $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.9-8.8 (m,5H of quinoline ring), 9.72(s, 1H, -NH), 10.20(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 148-$C_1$, 107-$C_2$, 116-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$, 148-$C_{7\&25}$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 143-$C_{10}$, 130-$C_{11}$, 132-$C_{12}$,

121-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 32-$C_{15}$, 74-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 135-$C_{19}$, 163-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$, 118-$C_{26}$(Indolering E&F).

**3.6.6.(Z)-2-((5-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxoindolin-3-ylidene)aceto - hydrazide (5f)**

IR(KBr): 1622(-C=N), 1179(C-S), 1695(NH-C=O), 1696(Thiazolidinone-C=O), 3126 (-NH), 3040cm$^{-1}$ (Ar-H str). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ= 4.71(s,2H,-O-$CH_2$), 6.52(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.9(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.4-8.8 (m,13H of $C_6H_4$ of phenyl, $C_6H_4$ of indole $C_9H_5N$ of quinoline), 9.70(s,1H,-NH), 10.20(s,1H,-NH of Indole). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 149-$C_1$, 108-$C_2$, 116-$C_3$, 134-$C_4$, 128-$C_5$, 121-$C_6$, 147-$C_{7\&25}$, 140-$C_8$, 123-$C_9$(quinoline ring A&B), 150-$C_{10}$, 128-$C_{11}$, 121-$C_{12}$, 146-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 33-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 70-$C_{17}$(O-$CH_2$), 134-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 129-$C_{24}$,117-$C_{26}$(Indole ring E&F).

**3.7. Synthesis of (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(4-substituted phenyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6a-h)**

A mixture of **(5a) (**0.1 mol), piperidine (0.15 mol) and water (20 mL) was stirred to obtain a clear solution. To this solution, HCHO (0.05mol) and DMF were added in ice-cold condition and stirred for 2 hours in an ice-bath and left overnight at room temperature. The obtained white solid was isolated and crystallized from ethanol to give Compound **(6a).** The reaction procedure leading to **(6a)** was then extended to the syntheses of **(6b-h).**

**3.7.1.(Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-phenyl thiazolidin-3-yl)quinolin-8-yl) oxy)acetohydrazide (6a)**

IR (KBr): 1613(-C=N), 1698 (Thiazolidinone-C=O), 1710(CO-NH), 1188(C-S), 3040 (Ar-H str), 3190cm$^{-1}$ (NH). $^1$HNMR(300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring), 4.6(s,2H,N-$CH_2$-N), 4.8(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.26-7.71(m, 9H $C_6H_5$ of phenyl, $C_6H_4$ of indole), 7.9-8.8 (m,5H of quinoline), 9.52(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 150-$C_1$, 107-$C_2$, 116-$C_3$, 134-$C_4$, 129-$C_5$, 121-$C_6$, 147-$C_{7\&25}$, 141-$C_8$, 122-$C_9$(quinoline ring A&B), 139-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$,130-$C_{24}$, 117-$C_{26}$(Indole ring E&F), 75-$C_{27}$(-N-$CH_2$-N), 55-$C_{28}$, 26-$C_{29}$ (Piperidine ring G).

**3.7.2.(Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)quinolin -8-yl)oxy)acetohydrazide (6b)**

IR (KBr): 1604(-C=N), 1696 (Thiazolidinone-C=O), 1702(CO-NH), 1179(C-S), 3041 (Ar-H str), 3189cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring), 2.34 (s, 3H, Ar-$CH_3$), 4.0(s,2H,N-$CH_2$-N), 4.83(s,2H,-O-$CH_2$), 6.42(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.81(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.20-7.78 (m, 8H $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.95-8.81 (m,5H of quinoline), 9.58(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 151-$C_1$, 107-$C_2$, 116-$C_3$, 133-$C_4$, 128-$C_5$, 120-$C_6$, 148-$C_{7\&25}$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 141-$C_{10}$, 127-$C_{11}$, 129-$C_{12}$, 136-$C_{13}$ (phenyl ring C), 169-$C_{14\&18}$, 35-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 133-$C_{19}$, 163-$C_{20}$, 122-$C_{21}$, 132-$C_{22}$, 125-$C_{23}$, 130-$C_{24}$, 117-$C_{26}$(Indole ring E&F), 76-$C_{27}$(-N-$CH_2$-N), 54-$C_{28}$, 26-$C_{29}$(Piperidine ring G), 21(Ar-$CH_3$).

**3.7.3.(Z)-2-((5-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-yl - methyl)indolin-3-ylidene)acetohydrazide (6c)**

IR (KBr): 1609(-C=N), 1697 (Thiazolidinone-C=O), 1696(CO-NH), 1166(C-S), 3040 (Ar-H str), 3180cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring), 3.73 (s, 3H, Ar-O-$CH_3$), 4.0(s,2H,N-$CH_2$-N), 4.78(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.78(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.1-7. 8 (m, 8H $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.98-8.82 (m,5H of quinoline), 9.54(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 151-$C_1$, 108-$C_2$, 116-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$, 149-$C_{7\&25}$, 140-$C_8$, 122-$C_9$(quinoline ring A&B), 136-$C_{10}$, 128-$C_{11}$, 114-$C_{12}$, 158-$C_{13}$ (phenyl ring C), 172-$C_{14\&18}$, 34-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 162-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$,118-$C_{26}$(Indole-ring E&F), 76-$C_{27}$(-N-$CH_2$-N), 54-$C_{28}$, 25-$C_{29}$(Piperidine ring G), 55(Ar-O-$CH_3$).

**3.7.4.(Z)-2-((5-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl) indolin-3-ylidene)acetohydrazide (6d)**

IR (KBr): 1602(-C=N), 1692(Thiazolidinone-C=O), 1704(CO-NH), 1179(C-S), 3042 (Ar-H str), 3185cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring),4.0(s,2H,N-$CH_2$-N), 4.78(s,2H,-O-$CH_2$), 6.38(s,1H,-CH of Thiazolidin attached to phenyl ring),

3.92(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.0-7.8 (m, 8H of $C_6H_4$, indole), 7.95-8.84 (m,5H of quinoline), 9.58(s, 1H, -NH) $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 150-$C_1$, 107-$C_2$, 117-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$,148-$C_{7\&25}$,139-$C_8$, 122-$C_9$(quinoline ring A&B), 141-$C_{10}$, 128-$C_{11}$,132-$C_{12}$,121-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 34-$C_{15}$, 72-$C_{16}$ (thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 163-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$,118-$C_{26}$(Indole ring E&F),75-$C_{27}$(-N-$CH_2$-N), 55-$C_{28}$, 25-$C_{29}$(Piperidine ring G).

**Table 1. Analytical data of the compounds 3a-f, 5a-f and 6a-f**

| Compound | Moleular formula | Yield (%) | M.P. * ($^0$C) | % Analysis | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | C | | H | | N | |
| | | | | Cald | Found | Cald | Found | Cald | Found |
| 3a | $C_{20}H_{18}N_4O_3S$ | 65 | 140-1 | 60.90 | 60.78 | 4.60 | 4.42 | 14.20 | 14.17 |
| 3b | $C_{21}H_{20}N_4O_3S$ | 60 | 162-3 | 61.75 | 61.52 | 4.94 | 4.76 | 13.72 | 13.64 |
| 3c | $C_{21}H_{20}N_4O_4S$ | 55 | 171-2 | 59.42 | 59.16 | 4.75 | 4.27 | 13.20 | 13.05 |
| 3d | $C_{20}H_{17}ClN_4O_3S$ | 70 | 196-7 | 56.01 | 55.64 | 4.00 | 3.71 | 13.06 | 12.72 |
| 3e | $C_{20}H_{17}BrN_4O_3S$ | 75 | 182-3 | 50.75 | 50.61 | 3.62 | 3.28 | 11.84 | 11.14 |
| 3f | $C_{20}H_{17}N_5O_5S$ | 60 | 215-6 | 54.66 | 54.48 | 3.90 | 3.72 | 15.94 | 15.28 |
| 5a | $C_{28}H_{21}N_5O_4S$ | 65 | 170-1 | 64.23 | 64.23 | 4.04 | 3.84 | 13.38 | 13.33 |
| 5b | $C_{29}H_{23}N_5O_4S$ | 60 | 193-4 | 64.79 | 64.56 | 4.31 | 4.18 | 11.90 | 11.72 |
| 5c | $C_{29}H_{23}N_5O_5S$ | 55 | 182-3 | 62.92 | 62.68 | 4.19 | 3.98 | 12.64 | 12.52 |
| 5d | $C_{28}H_{20}ClN_5O_4S$ | 62 | 205-6 | 60.27 | 59.97 | 3.61 | 3.52 | 12.55 | 12.34 |
| 5e | $C_{28}H_{20}BrN_5O_4S$ | 60 | 216-7 | 55.82 | 55.52 | 3.35 | 3.26 | 11.62 | 11.48 |
| 5f | $C_{28}H_{20}N_6O_6S$ | 60 | 228-9 | 59.15 | 58.98 | 3.55 | 3.28 | 14.78 | 14.46 |
| 6a | $C_{34}H_{32}N_6O_4S$ | 60 | 156-7 | 65.79 | 65.62 | 5.20 | 5.14 | 13.54 | 13.41 |
| 6b | $C_{35}H_{34}N_6O_4S$ | 65 | 183-4 | 66.23 | 66.18 | 5.40 | 5.18 | 13.24 | 13.05 |
| 6c | $C_{34}H_{31}N_6O_5S$ | 60 | 168-9 | 64.60 | 64.98 | 5.27 | 5.08 | 12.91 | 12.78 |
| 6d | $C_{34}H_{31}ClN_6O_4S$ | 70 | 190-1 | 62.33 | 62.12 | 4.77 | 4.61 | 12.83 | 12.74 |
| 6e | $C_{34}H_{31}BrN_6O_4S$ | 70 | 212-3 | 58.37 | 58.37 | 4.47 | 4.29 | 12.01 | 11.94 |
| 6f | $C_{34}H_{31}N_7O_6S$ | 74 | 240-1 | 61.34 | 61.10 | 4.69 | 4.52 | 14.73 | 14.48 |
| 6g | $C_{33}H_{30}N_6O_5S$ | 60 | 148-9 | 63.65 | 63.52 | 4.86 | 4.53 | 13.50 | 13.18 |
| 6h | $C_{34}H_{33}N_7O_4S$ | 65 | 161-2 | 64.23 | 64.06 | 5.23 | 5.19 | 15.42 | 15.31 |

**Table 2.Antibacterial Activity by the disc diffusion method**

| S.No | Compound | Zone of Inhibition | | | |
|---|---|---|---|---|---|
| | | *Staphylococcus aureus* | *Bacillus Cereus* | *Escherichia Coli* | *Pseudomonas aeruginosa* |
| 1 | (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6a) | 08 | 07 | 05 | 06 |
| 2 | (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6b) | 07 | 06 | 06 | 07 |
| 3 | (Z)-2-((5-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6c) | 07 | 06 | 06 | 07 |
| 4 | (Z)-2-((5-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6d) | 10 | 09 | 08 | 10 |
| 5 | (Z)-2-((5-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6e) | 09 | 08 | 07 | 09 |
| 6 | (Z)-2-((5-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6f) | 12 | 11 | 09 | 10 |
| 7 | (Z)-N'-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6g) | 11 | 10 | 08 | 09 |
| 8 | (Z)-N'-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6h) | 10 | 09 | 08 | 08 |
| 9 | Cefaclor | 19 | 22 | 19 | 20 |

** indicate diameter of inhibition in mm.*

**3.7.5.(Z)-2-((5-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-yl -methyl)indolin-3-ylidene)acetohydrazide (6e)**

IR (KBr): 1600(-C=N), 1694(Thiazolidinone-C=O), 1710(CO-NH), 1168(C-S), 3040 (Ar-H str), 3178cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring), 4.0(s,2H,N-$CH_2$-N), 4.78(s,2H,-O-$CH_2$), 6.48(s,1H,-CH of Thiazolidin attached to phenyl ring), 4.1(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.05-7.78 (m, 8H $C_6H_4$ of phenyl, $C_6H_4$ of indole), 7.9-8.8 (m,5H of

quinoline ring), 9.58(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 150-$C_1$, 107-$C_2$, 116-$C_3$, 133-$C_4$, 128-$C_5$, 121-$C_6$, 148-$C_{7\&25}$, 139-$C_8$, 122-$C_9$(quinoline ring A&B), 143-$C_{10}$, 126-$C_{11}$, 132-$C_{12}$, 121-$C_{13}$ (phenyl ring C), 171-$C_{14\&18}$, 32-$C_{15}$, 74-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 163-$C_{20}$, 121-$C_{21}$, 131-$C_{22}$, 124-$C_{23}$, 129-$C_{24}$, 118-$C_{26}$(Indole ring E&F), 75-$C_{27}$(-N-$CH_2$-N), 55-$C_{28}$, 25-$C_{29}$(Piperidine ring-G).

**3.7.6.(Z)-2-((5-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl) -indolin-3-ylidene)acetohydrazide (6f)**

IR (KBr): 1600(-C=N), 1692(Thiazolidinone-C=O), 1724(CO-NH), 1169(C-S), 3040 (Ar-H str), 3186cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 1.30–1.51 [m, 6H $(CH_2)_3$ of piperidine ring], 2. 10 (t, 4H, –$CH_2$–N–$CH_2$ of piperidine ring), 4.0(s,2H,N-$CH_2$-N), 4.83(s,2H,-O-$CH_2$), 6.52(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.9(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.4-8.8 (m,13H $C_6H_4$ of phenyl, $C_6H_4$ of indole $C_9H_5N$ of quinolinne), 9.58(s,1H,-NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 152-$C_1$, 108-$C_2$, 116-$C_3$, 134-$C_4$, 129-$C_5$, 121-$C_6$, 149-$C_{7\&25}$, 140-$C_8$, 123-$C_9$(quinoline ring A&B), 150-$C_{10}$, 128-$C_{11}$, 121-$C_{12}$, 146-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 33-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 70-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 130-$C_{24}$,117-$C_{26}$(Indole ring E&F),75-$C_{27}$(-N-$CH_2$-N), 55-$C_{28}$, 26-$C_{29}$ (Piperidine ring G).

**3.7.7.(Z)-N'-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenyl thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6g)**

IR (KBr): 1604(-C=N), 1692(Thiazolidinone-C=O), 1694(CO-NH), 1185(C-S), 3042(Ar-H str), 3183cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 3.52 (t, 4H, –$CH_2$–O–$CH_2$ of morpholine ring), 2.45 (t, 4H, –$CH_2$–N–$CH_2$ of morpholine ring), 4.0(s,2H,N-$CH_2$-N),4.8(s,2H,-O-$CH_2$), 6.44(s,1H,-CH of Thiazolidin attached to phenyl ring), 3.85(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.26-7.81(m, 9H of $C_6H_5$ of phenyl, $C_6H_4$ of indole), 8.94-8.75 (m,5H of quinoline ring), 9.52(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ: 150-$C_1$, 107-$C_2$, 115-$C_3$, 134-$C_4$, 129-$C_5$, 121-$C_6$, 149-$C_{7\&25}$, 140-$C_8$, 122-$C_9$(quinoline ring A&B), 143-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$(phenyl ring C), 171-$C_{14\&18}$, 33-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 130-$C_{24}$, 117-$C_{26}$(Indole ring E&F), 75-$C_{27}$(-N-$CH_2$-N), 53-$C_{28}$, 66-$C_{29}$(Morpholine-G).

**3.7.8.(Z)-N'-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6h)**

IR (KBr): 1618(-C=N), 1694(Thiazolidinone-C=O), 1698(CO-NH), 1168(C-S), 3040(Ar-H str), 3188cm$^{-1}$ (NH). $^1$HNMR (300MHZ, $(CD)_2SO$, TMS): δ 2.2(s,3H,-N-CH3 of piperizine ring), 2.46(t,4H, , –$CH_2$–N–$CH_2$of piperizine ring), 2.32 (t, 4H, –$CH_2$–N($CH_3$)–$CH_2$), 4.1(s,2H,N-$CH_2$-N),4.8(s,2H,-O-$CH_2$), 6.52 (s,1H,-CH of Thiazolidin attached to phenyl ring), 3.92(s,2H,-$CH_2$ of Thiazolidin attached to –S), 7.21-7.8(m, 9H $C_6H_5$ of phenyl, $C_6H_4$ of indole), 8.1-8.8 (m,5H of quinoline ring), 9.58(s, 1H, -NH). $^{13}$C NMR (75 MHz, $CDCl_3$,TMS) δ = 152-$C_1$, 107-$C_2$, 116-$C_3$, 134-$C_4$, 129-$C_5$, 121-$C_6$, 149-$C_{7\&25}$, 140-$C_8$, 122-$C_9$(quinoline ring A&B), 143-$C_{10}$, 126-$C_{11}$, 129-$C_{12}$, 127-$C_{13}$ (phenyl ring C), 170-$C_{14\&18}$, 33-$C_{15}$, 73-$C_{16}$(thiazolidinone ring D), 69-$C_{17}$(O-$CH_2$), 132-$C_{19}$, 164-$C_{20}$, 122-$C_{21}$, 131-$C_{22}$, 125-$C_{23}$, 130-$C_{24}$, 117-$C_{26}$(Indole ring E&F), 75-$C_{27}$(-N-$CH_2$-N), 53-$C_{28}$, 57-$C_{29}$(N-Methyl piperazine ring G), 46(N-$CH_3$).

**Table 3. Antifungal Activity by the disc diffusion method**

| S.No | Compound | Zone of Inhibition | |
|---|---|---|---|
| | | *Asperigillus flavus* | *Candida albicans* |
| 1 | (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6a) | 12 | 16 |
| 2 | (Z)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)-2-((5-(4-oxo-2-(p-tolyl)thiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6b) | 17 | 19 |
| 3 | (Z)-2-((5-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6c) | 11 | 17 |
| 4 | (Z)-2-((5-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6d) | 18 | 19 |
| 5 | (Z)-2-((5-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6e) | 17 | 18 |
| 6 | (Z)-2-((5-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)quinolin-8-yl)oxy)-N'-(2-oxo-1-(piperidin-1-ylmethyl)indolin-3-ylidene)acetohydrazide (6f) | 19 | 20 |
| 7 | (Z)-N'-(1-(morpholinomethyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6g) | 20 | 19 |
| 8 | (Z)-N'-(1-((4-methylpiperazin-1-yl)methyl)-2-oxoindolin-3-ylidene)-2-((5-(4-oxo-2-phenylthiazolidin-3-yl)quinolin-8-yl)oxy)acetohydrazide (6h) | 18 | 17 |
| 9 | Clotrimazole | 25-30 | 25-30 |

**indicate diameter of inhibition in mm.*

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