

## Design, synthesis, characterization and biological evaluation of 3-(4-(7-chloro-2-(4-chlorophenyl)-4-oxo-quinazolin-3(4H)-yl)phenyl)-2-aryl 1,3-thiazolidin-4-ones as a new class of antimicrobial agents

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**Abstract:** Novel thiazolidinone derivatives TQ-VI(1-10) were designed, synthesized and screened for antimicrobial activity. Synthesis of 3-(4-(7-chloro-2-(4-chlorophenyl) 4-oxo-quinazolin-3(4H)-yl) phenyl) - 2-arylthiazolidin-4-one TQ-VI(1-10) have been achieved from the starting material 2-amino-4-chlorobenzoic acid TQ-I on cyclization with p-chlorobenzoyl chloride TQ-II to yield 7-chloro-2-(4-chlorophenyl)-4H-3,1-benzoxazin-4-one, TQ-III, which on treatment with p-phenylindiamine gave 3-(4-aminophenyl)-7-chloro-2-(4-chlorophenyl)quinazolin-4(3H)-one, TQ-IV in good yield. Then, TQ-IV on reaction with substituted aromatic aldehydes converted to TQ-V(1-10), which on cyclization with thioglycolic acid gave TQ-VI (1-10). All the synthesized compounds have been characterized on the basis of IR, <sup>1</sup>H-NMR and mass spectral data. The compounds containing 4-OH, 4-OCH<sub>3</sub> and 3,4,5-(OCH<sub>3</sub>)<sub>3</sub> showed good activity. The title compounds were screened for qualitative (zone of inhibition) and quantitative antimicrobial activity (MIC) by agar cup plate method and serial dilution technique, respectively. Among the synthesized compounds in the series, the compound TQVI4 and TQVI5 were found to exhibit significant antifungal activity at lower concentration of 31.25 µg/ml, against *A.niger*. The compound TQVI5 and TQVI4 showed zone of inhibition of 17mm and 15mm against *A.niger* and *C.albicans* respectively which is comparable to that of standard drug. The rest of the analogues in the series displayed weak to moderate antimicrobial activity when compared to the standard positive controls Ampicillin and Amphotericin B.

**Key Words:** Thiazolidinone, quinazolinone, benzoxazinone, synthesis, characterization.

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### I. Introduction

The usage of most of the antimicrobial agents is limited, not only by the rapidly developing drug resistance, but also by the unsatisfactory status of present treatments of bacterial and fungal infections and drug side effects. This has spurred the scientists to develop the new antibacterial agents having broad antimicrobial spectrum. In the present research work we reported the synthesis of some new thiazolidinone derivatives by using various substituted aromatic aldehydes and screened for their anti-microbial activity. Thiazolidinones are derivatives of thiazolidine and are significant group of heterocyclic compounds. There are three types of thiazolidinones based on 2<sup>nd</sup>, 4<sup>th</sup> and 5<sup>th</sup> position of carbonyl group. The most significant one is thiazolidinone with carbonyl group at 4<sup>th</sup> position, which is also known as 4-thiazolidinone or 4-oxo-thiazolidine. Thiazolidin-4-ones and their derivatives have attracted much attention due to diverse biological activities such as antidiabetic<sup>1</sup>, antihistaminic<sup>2,3</sup>, Ca<sup>2+</sup>-channel blocker<sup>4</sup>, anti-platelet activating factor<sup>5,6</sup>, anti-diarrheal<sup>7</sup>, platelet activating factor (PAF) antagonist<sup>8</sup>, cardioprotective<sup>9</sup>, anti-ischemic<sup>10</sup>, cyclooxygenase (COX) inhibitory<sup>11</sup>, anti-cancer<sup>12</sup>, nematocidal<sup>13</sup> and convulsant<sup>14</sup> activities. Quinazolinone is an important heterocyclic ring with broad spectrum of biological activities like anticonvulsant<sup>15</sup>, analgesic<sup>16</sup>, antitumor<sup>17</sup>, anti-inflammatory<sup>18</sup>, antimicrobial<sup>19</sup>, antitubercular<sup>20</sup>, antioxidant<sup>21</sup> and antiviral<sup>22</sup> activities. In view of antimicrobial activities of some thiazolidinone derivatives and quinazolinone derivatives it was of curiosity to couple these two moieties with the hope that the resulting compounds might exhibit superior activity. After a comprehensive literature survey our focus was to synthesise thiazolidinone derivatives as less toxic, more active antimicrobial agents (Fig. 1). The synthetic strategies adopted for the synthesis of the intermediate and target compounds are depicted in the Scheme I.

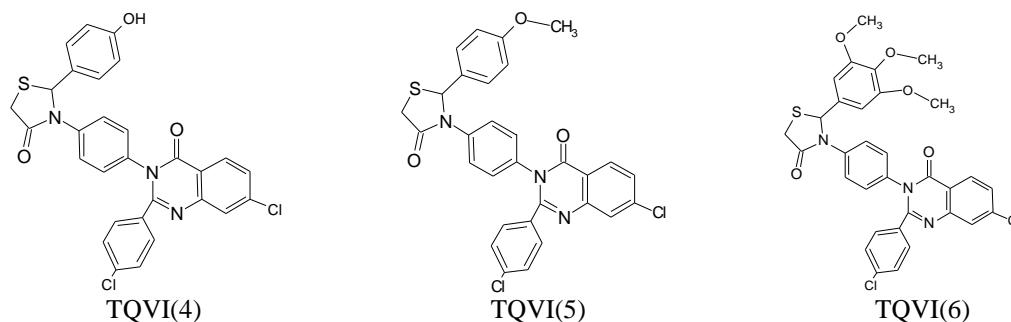
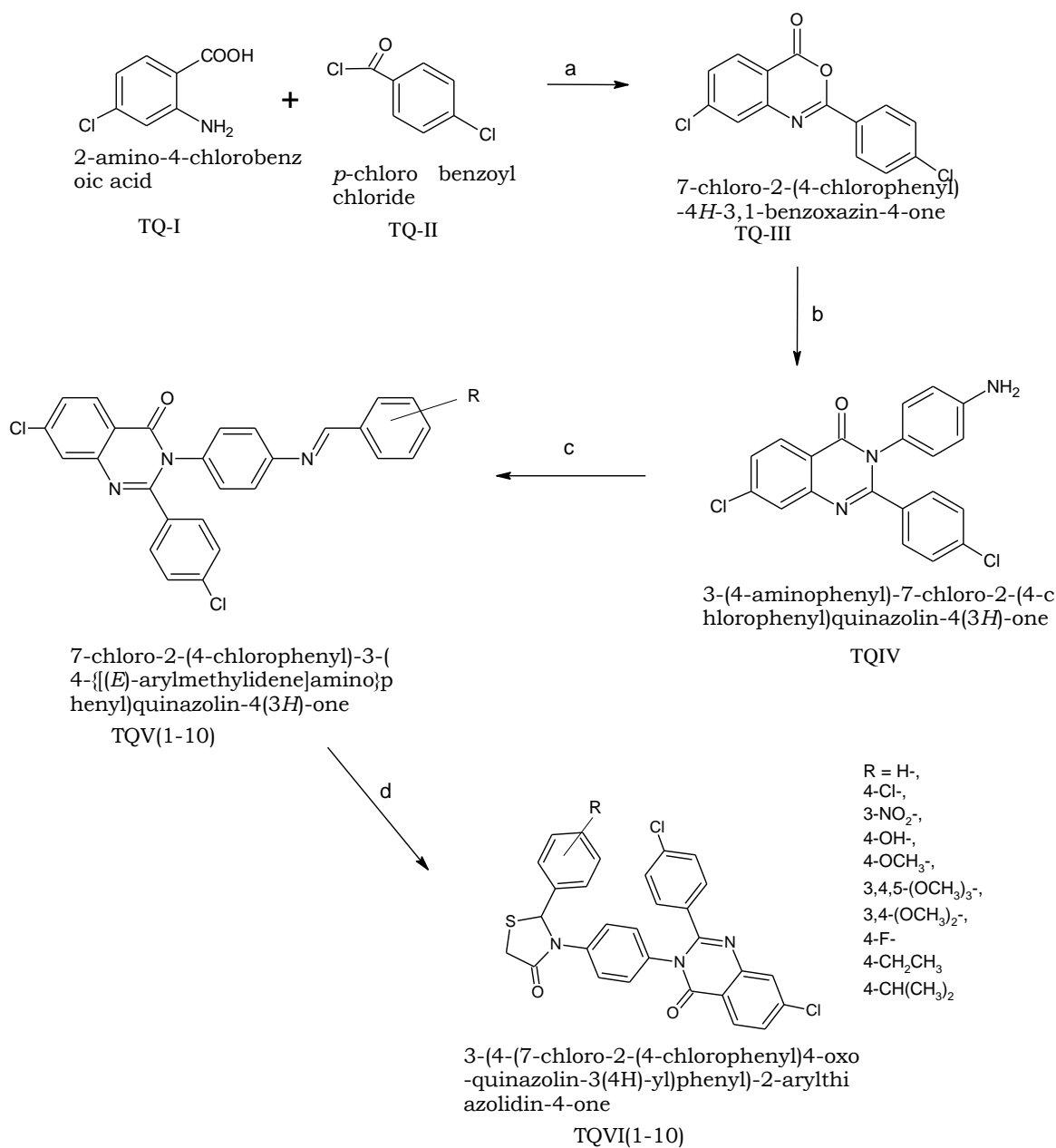


Figure 1. Structures of the most active compounds.



Scheme I. Reagents and condition: (a) Pyridine, NaHCO<sub>3</sub>, Stirr for 30min; (b) Pyridine,HCl, *p*-phenylenediamine, Reflux for 6h; (c) aryl aldehyde, Ethanol, Glacial acetic acid, Reflux for 8h; (d) DMF, ZnCl<sub>2</sub>, HSCH<sub>2</sub>COOH, Reflux for 8h;

## II. Materials And Methods

In the present study the title compounds were examined for in vitro antimicrobial potency against four bacterial pathogens and two fungal pathogens. Bacterial and fungal strains (Microbial Type Culture Collection, MTCC) were purchased from IMTECH, Chandigarh, India. Ampicillin and Amphotericin B were procured from Sigma Aldrich, Bangalore, India. Samples were routinely purified by crystallization from ethanol. Melting points were taken in open capillaries and are uncorrected. The purity of compounds was checked by TLC on silica gel 'G' coated glass plates. IR spectra were recorded in BRUKER ATR-IR spectrophotometer. <sup>1</sup>H-NMR spectra (DMSO) were recorded on NEW AVANCE- (300 MHz) NMR spectrometer using TMS as internal standard. Mass spectra of the synthesized compounds have been recorded on a VG Autospec MS using ESI<sup>+</sup> software with capillary voltage 3.98 kV and ESI mode positive ion trap detector. Chloroform and ethylacetate in the ratio 7:3 was used as mobile phase for elution and the spots were detected in iodine chamber.

## III. Experimental

General procedure for synthesis of 7-chloro-2-(4-chlorophenyl)-4H-3, 1-benzoxazin-4-one TQ-III<sup>23,24</sup>: 2-Amino-4-chlorobenzoic acid (0.1 mol) was dissolved in 30ml of dry pyridine by stirring slowly at room temperature. The solution was cooled to 0°C and a solution of a p-chloro benzoyl chloride (0.2 mol) in 30ml of dry pyridine was added slowly with constant stirring. After this addition the reaction mixture was further stirred for half an hour at room temperature and set aside for 1h. The pasty mass obtained was diluted with 50 ml of water and treated with aqueous sodium bicarbonate solution. When the effervescence ceased, the precipitate obtained was filtered and washed with water. The crude 7-chloro-2-(4-chlorophenyl)-4H-3, 1-benzoxazin-4-one obtained was dried and recrystallized from diluted ethanol (m.p:155-157), yield (92%).

**General procedure for synthesis of 3-(4-aminophenyl)-7-chloro-2-(4-chlorophenyl)-quinazolin-4(3H)-one TQ-IV<sup>25</sup>**: 7-chloro-2-(4-chlorophenyl)-4H-3,1-benzoxazin-4-one (0.01mol) and p-phenylenediamine (1.08 g, 0.01 mol) was dissolved in 50 mL of anhydrous pyridine and refluxed for 6 h. The resulting solution was cooled in ice bath and treated with 100 mL of dilute hydrochloric acid. The obtained crude precipitate of 3-(4-aminophenyl)-7-chloro-2-(4-chlorophenyl)quinazolin-4(3H)-one was filtered, washed with water and recrystallized from ethanol (m.p:165-167), yield (85-90%).

**General procedure for synthesis of 7-chloro-2-(4-chlorophenyl)-3-(4-[(E)-arylmethylidene] amino} phenyl) quinazolin-4(3H)-one TQ-V (1-10)<sup>26</sup>**: 3-(4-aminophenyl)-7-chloro-2-(4-chlorophenyl) quinazolin-4(3H)-one TQ-IV (0.01 mol) and aromatic aldehydes (0.01 mol) were dissolved in absolute ethanol (50 ml), by the addition of a few drops of glacial acetic acid. The reaction mixture was refluxed for 8h. The reaction mixture was allowed to cool and poured into ice cold water. The separated solid was filtered, washed and recrystallized from ethanol.

**General procedure for the synthesis of 3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3(4H)-yl)phenyl)-2-arylthiazolidin-4-one TQ-VI(1-10)<sup>27</sup>**: 7-chloro-2-(4-chlorophenyl)-3-(4-[(E)-arylmethylidene] amino} phenyl) quinazolin-4(3H)-one TQ-V (A-G) (0.01 mol) were dissolved in dry DMF (50 ml), containing a pinch of anhydrous ZnCl<sub>2</sub> and thioglycolic acid (0.02 mol) and refluxed for about 8h. Excess of solvent was distilled off and the residual reaction mixture cooled and poured into ice cold water. The separated solid was filtered, washed and recrystallized from ethanol.

## IV. Results And Discussions

**Spectral data of synthesized compounds TQVI (1-10):**

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3(4H)-yl)phenyl)-2-phenyl thiazolidin-4-one TQVI(1)**: ATR-IR ( $\nu_{\max}$  cm<sup>-1</sup>): 1730 -C=O stretching; 1662 -C=O stretching; 1517 -C=N stretching; 3085 -C-H aromatic stretching; 812 -C-Cl stretching; 1370 -NCS stretching; <sup>1</sup>HNMR  $\delta$ ppm 300 MHz, DMSO-d<sub>6</sub>:  $\delta$ 5.9 (s, -CH-Ar, 1H),  $\delta$ 3.7 (s, -CH<sub>2</sub>-S- 2H),  $\delta$ 6.7-8.8 (m, Ar-H and quinazoline-H, 16H). MS: m/z 544(M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)-4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(4-chlorophenyl) thiazolidin-4-one TQVI(2)**: ATR-IR ( $\nu_{\max}$  cm<sup>-1</sup>): 1703 -C=O stretching; 1665 -C=O stretching; 1519 -C=N stretching; 3093 -C-H aromatic stretching; 816 C-Cl stretching; 1363 -NCS stretching; <sup>1</sup>HNMR  $\delta$ ppm 300 MHz, DMSO-d<sub>6</sub>:  $\delta$ 6.0 (s, -CH-Ar, 1H),  $\delta$ 3.5 (s, -CH<sub>2</sub>-S, 2H),  $\delta$ 6.3-9.0 (m, Ar-H, 15H and quinazoline-H) MS: m/

**3-(4-(7-chloro-2-(4-chlorophenyl)-4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(3-nitrophenyl) thiazolidin-4-one (TQVI(3))**: ATR-IR ( $\nu_{\max}$  cm<sup>-1</sup>): 1730 -C=O stretching; 1661 -C=O stretching; 1510 -C=N stretching; 3049 -C-H Aromatic stretching; 812 -C-Cl stretching; 1377 -N-C-S stretching; <sup>1</sup>HNMR  $\delta$ ppm 300 MHz, DMSO-d<sub>6</sub>:  $\delta$ 6.2 (s, 1H, -CH-Ar), 3.4(s, 2H, -CH<sub>2</sub>-S-),  $\delta$ 7.2-8.9 (m, Ar-H and quinazoline-H, 15H) MS: m/z 589 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(4-hydroxyphenyl) thiazolidin-4-one TQVI(4)**: ATR-IR ( $\nu_{\max}$  cm<sup>-1</sup>): 1740 -C=O stretching; 1654 -C=O stretching; 1503 -C=N stretching; 3074 -C-H aromatic stretching; 827 -C-Cl stretching; 3389 -OH stretching; 1242 -N-C-S) stretching;

<sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ6.1 (s, 1H, -CH-Ar), δ3.7 (s, 2H, -CH<sub>2</sub>-S-), δ6.4-8.3 (m, Ar-H and quinazoline -H, 15H) MS: m/z 526 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl) 4-oxo-quinazolin-3-(4H)-yl) phenyl)-2-(4-methoxyphenyl) thiazolidin-4-one TQVI(5):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 1736 -C=O stretching; 1656 -C=O stretching; 1504 -C=N stretching; 1504 -C=C stretching; 3085 -C-H aromatic stretching; 2920, 2851-C-H aliphatic stretching; 826 -C-Cl stretching; 1243 -C-O-C stretching; 1362 -N-C-S stretching; <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ6.4 (s, -CH-Ar, 1H), δ3.3 (s, -CH<sub>2</sub>-S, 2H), δ6.7-8.8 (m, Ar-H and quinazoline-H, 15H), δ2.7 (s, -OCH<sub>3</sub>, 3H) MS: m/z 574 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(3,4,5-trimethoxyphenyl) thiazolidin-4-one TQVI(6):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 3089 -C-H aromatic stretching; 2917,2848 -C-H aliphatic stretching; 1741 -C=O stretching; 1655 -C=O stretching; 1504 -C=N stretching; 826 -C-Cl stretching; 1244 -C-O-C stretching; 1362 -N-C-S stretching; <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ6.0 (s, -CH-Ar, 1H), δ3.9 (s, -CH<sub>2</sub>-S, 2H), δ6.5-8.4 (m, Ar-H and quinazoline-H, 13H) δ2.5 (s, 9H, -(OCH<sub>3</sub>)<sub>3</sub>). MS: m/z 635 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(3,4-dimethoxyphenyl) thiazolidin-4-one TQVI(7):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 3067 -C-H aromatic stretching; 2932,2873 -C-H aliphatic stretching; 1729 -C=O stretching; 1636 -C=O stretching; 1505 -C=N stretching; 831 -C-Cl stretching; 1244 -C-O-C stretching; 1373 -N-C-S stretching; <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ5.9 (s, -CH-Ar, 1H), δ4.0 (s, CH<sub>2</sub>-S, 2H), δ6.5-8.0 (m, Ar-H and quinazoline-H, 15H) δ2.5 (s, 6H, -(OCH<sub>3</sub>)<sub>2</sub>). MS: m/z 605 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(4-fluorophenyl) thiazolidin-4-one TQVI(8):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 1736 -C=O stretching, 1656 -C=O stretching, 1504 -C=N stretching, 3075 -C-H aromatic stretching, 826 -C-Cl stretching, 1362 -NCS stretching. <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ5.9 (s, -CH-Ar, 1H), δ3.7 (s, CH<sub>2</sub>-S, 2H), δ7.0-9.0 (m, Ar-H and quinazoline-H, 15H) MS: m/z 562 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(4-ethylphenyl) thiazolidin-4-one TQVI(9):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 3055 -C-H aromatic stretching; 2964,2837 -C-H aliphatic stretching; 1703 -C=O stretching; 1693 -C=O stretching; 823 -C-Cl stretching; 1244 -C-O-C stretching; 1322 -N-C-S stretching; <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ5.8 (s, -CH-Ar, 1H), δ3.0 (s, -CH<sub>2</sub>-S, 2H), δ6.2-8.0 (m, Ar-H and quinazoline-H, 15H), δ2.1-2.4 (q, -CH<sub>2</sub>, 2H), δ1.7 (t, -CH<sub>3</sub>, 3H). MS: m/z 573 (M<sup>+</sup>).

**3-(4-(7-chloro-2-(4-chlorophenyl)4-oxo-quinazolin-3-(4H)-yl)phenyl)-2-(4-isopropylphenyl) thiazolidin-4-one TQVI(10):** ATR-IR (ν<sub>max</sub> cm<sup>-1</sup>): 3097 -C-H aromatic stretching; 2916,2794 -C-H aliphatic stretching; 1745 -C=O stretching; 1662 -C=O stretching; 825 -C-Cl stretching; 1260 -C-O-C stretching; 1320 -N-C-S stretching; <sup>1</sup>HNMR δppm 300 MHz, DMSO-d<sub>6</sub>: δ5.8 (s, -CH-Ar, 1H), δ3.9 (s, -CH<sub>2</sub>-S, 2H), δ7.0-8.4 (m, Ar-H and quinazoline-H, 15H), δ2.0 (s, -N(CH<sub>3</sub>)<sub>2</sub>, 6H). MS: m/z 588 (M<sup>+</sup>).

#### **Antimicrobial activity - cup plate method<sup>28</sup>**

The antimicrobial screening of synthesized compounds was performed using the cup plate method. Nutrient broth media and Sabouraud's dextrose was prepared sterilized by autoclaving and was transferred into sterile Petri plates. After solidification of media, cups of diameter 8mm were made with a sterile cork borer. 200 μl of the standardized<sup>29</sup> bacterial inoculums and fungus inoculums containing about 3.0 × 10<sup>5</sup> cfu/ml were spread on medium using bent glass rod. The synthesized compounds were dissolved in DMF to get a final concentration 100μg/0.1ml and tested for activity. Ampicillin and Amphotericin B were used as a standard for the antibacterial and antifungal activity, respectively. All the bacterial Petri plates were kept in incubator at 37±1°C and the fungal Petri plate was in an incubator at 24±1°C. Then the zones of inhibition of bacterial and fungal growth were measured by using a transparent ruler.

Antibacterial and antifungal activity of all the synthesized compounds was screened against two gram-positive bacterial strains (*S.aureus* & *B.subtilis*) and two gram-negative (*E.coli* & *P.aeruginosa*) bacterial strains, two fungal strains (*A.niger* & *C.albicans*) at a concentration of 100 μg/0.1ml using cup plate method. The MIC level of compounds TQ-VI (1-10) against these organisms is given in Table 2. The screening results of antibacterial activities showed that the compound with TQ-VI4, TQ-VI5, TQ-VI6 with 4-OH, 4-OCH<sub>3</sub> and 3,4,5-(OCH<sub>3</sub>)<sub>3</sub> substituent's respectively showed potent activity against *A.niger*. Compound TQ-VI4 bearing 4-OH substituent showed good activity against *C.albicans*. Compounds TQ-VI2, TQ-VI5 with 4-Cl and 4-OCH<sub>3</sub> substituent's showed good activity against *E.Coli* and *P.aeruginosa*. Other compounds showed mild to moderate antibacterial and antifungal activity. Structure of compounds TQ-V (1-10) and TQ-VI (1-10) was established on the basis of spectral data. The IR spectra of TQ-VI (1-10) showed absence of absorption in the region 1500-1525 cm<sup>-1</sup> which confirms the absence of -CH=N- and presence of absorption band in the range 1730-1740 cm<sup>-1</sup> due to C=O of thiazolidinone. <sup>1</sup>H NMR spectra of compounds TQ-V (1-10) showed a singlet of -N=CH- at 6.00, and presence of a singlet of -CH<sub>2</sub>-S- at 3.65 in compounds TQ-VI (1-10) confirms the formation of TQ-VI (1-10).

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### V. Conclusion

In the present paper, we report the synthesis, spectral studies, evaluation of antimicrobial activity of 3-(4-(7-chloro-2-(4-chlorophenyl)-4-oxo-quinazolin-3-(4H)-yl) phenyl)-2-arylthiazolidin-4-one TQ-VI(1-10). Thus these compounds constitute an interesting template for the evaluation of antimicrobial activity. In conclusion, we reported herein a simple and convenient route for the synthesis of some new heterocyclic compounds based on thiazolidinone for antimicrobial evaluation.

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**Table-1:** Physicochemical Characterization Of Newly Synthesized Compounds TQ-V (1-10) And TQ-VI (1-10)

Compound	Molecular formula	Molecular Weight	Melting point (°C)	% yield	R <sub>f</sub> value
TQV(1)	C <sub>27</sub> H <sub>17</sub> C <sub>12</sub> N <sub>3</sub> O	470.3	144-145	75	0.69
TQV(2)	C <sub>27</sub> H <sub>16</sub> C <sub>13</sub> N <sub>3</sub> O	504.7	216-217	78	0.71
TQV(3)	C <sub>27</sub> H <sub>16</sub> C <sub>12</sub> N <sub>4</sub> O <sub>3</sub>	515.3	168-169	70	0.73
TQV(4)	C <sub>27</sub> H <sub>17</sub> C <sub>12</sub> N <sub>3</sub> O <sub>2</sub>	486.3	188-189	67	0.63
TQV(5)	C <sub>28</sub> H <sub>19</sub> C <sub>12</sub> N <sub>3</sub> O <sub>2</sub>	500.3	286-287	73	0.68
TQV(6)	C <sub>30</sub> H <sub>23</sub> C <sub>12</sub> N <sub>3</sub> O <sub>4</sub>	560.4	256-257	75	0.65
TQV(7)	C <sub>29</sub> H <sub>21</sub> C <sub>12</sub> N <sub>3</sub> O <sub>3</sub>	530.4	252-253	78	0.78
TQV(8)	C <sub>27</sub> H <sub>16</sub> C <sub>12</sub> FN <sub>3</sub> O	488.3	190-191	82	0.70
TQV(9)	C <sub>29</sub> H <sub>21</sub> C <sub>12</sub> N <sub>3</sub> O	498.4	264-265	71	0.62
TQV(10)	C <sub>29</sub> H <sub>22</sub> C <sub>12</sub> N <sub>4</sub> O	513.42	162-163	74	0.59
TQVI(1)	C <sub>29</sub> H <sub>19</sub> C <sub>12</sub> N <sub>3</sub> O <sub>2</sub> S	544.4	180-181	60	0.60
TQVI(2)	C <sub>29</sub> H <sub>18</sub> C <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	578.8	246-247	67	0.82
TQVI(3)	C <sub>29</sub> H <sub>18</sub> C <sub>12</sub> N <sub>4</sub> O <sub>4</sub> S	589.4	212-213	64	0.79
TQVI(4)	C <sub>29</sub> H <sub>19</sub> C <sub>12</sub> N <sub>3</sub> O <sub>3</sub> S	560.4	282-283	65	0.45
TQVI(5)	C <sub>30</sub> H <sub>21</sub> C <sub>12</sub> N <sub>3</sub> O <sub>3</sub> S	574.4	270-271	67	0.50
TQVI(6)	C <sub>32</sub> H <sub>25</sub> C <sub>12</sub> N <sub>3</sub> O <sub>5</sub> S	634.5	260-261	66	0.47
TQVI(7)	C <sub>31</sub> H <sub>23</sub> C <sub>12</sub> N <sub>3</sub> O <sub>4</sub> S	604.5	220-221	61	0.52
TQVI(8)	C <sub>29</sub> H <sub>18</sub> C <sub>12</sub> FN <sub>3</sub> O <sub>2</sub> S	562.4	230-231	74	0.80
TQVI(9)	C <sub>31</sub> H <sub>23</sub> C <sub>12</sub> N <sub>3</sub> O <sub>2</sub> S	572.5	252-253	56	0.75
TQVI(10)	C <sub>31</sub> H <sub>24</sub> C <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S	587.52	196-197	67	0.48

**Table 2:** In Vitro Antibacterial And Antifungal Activity (Quantitative Study) Of The Synthesized Compounds TQ-VI(1-10)

Compound	R	Antibacterial Activity (MIC <sup>a</sup> in µg/ml)					
		S.aureus <sup>b</sup>	B.subtilis <sup>b</sup>	E.coli <sup>b</sup>	P.aeruginosa <sup>b</sup>	A.niger <sup>c</sup>	C.albicans <sup>c</sup>
TQVI(1)	H-	500	1000	500	500	500	500
TQVI(2)	4-Cl-	500	500	250	125	500	125
TQVI(3)	3-NO <sub>2</sub> -	500	1000	1000	1000	125	500
TQVI(4)	4-OH-	500	1000	500	500	31.25	62.5
TQVI(5)	4-OCH <sub>3</sub> -	250	125	125	62.5	31.25	125
TQVI(6)	3,4,5-(OCH <sub>3</sub> ) <sub>3</sub> -	125	125	125	62.5	62.5	125
TQVI(7)	3,4-(OCH <sub>3</sub> ) <sub>2</sub> -	125	125	500	125	62.5	125
TQVI(8)	4-F-	250	500	125	125	125	62.5
TQVI(9)	4-CH <sub>2</sub> CH <sub>3</sub>	500	1000	500	1000	62.5	250
TQVI(10)	4-CH(CH <sub>3</sub> ) <sub>2</sub>	500	500	1000	1000	62.5	62.5
DMF <sup>d</sup>	-	-	-	-	-	-	-
Ampicillin	-	1.95	1.95	7.81	15.62	-	-
Amphotericin B	-	-	-	-	-	3.90	7.81

<sup>a</sup> The MIC value is defined as lowest concentration of the antifungal agent exhibiting no fungal growth. <sup>b</sup> Bacteria tested: Staphylococcus aureus (MTCC 3160) and Bacillus subtilis (MTCC 441). Escherichia coli (MTCC 443) and Pseudomonas aeruginosa (MTCC 424).

<sup>c</sup> Fungi tested : Aspergillus niger (MTCC 282) and Candida albicans (MTCC 227)

<sup>d</sup> DMF: Dimethyl formamide.

**TABLE 3:** In Vitro Antibacterial And Antifungal Activity (Qualitative Study) Of The Synthesized Compounds TQ-VI(1-10)

Compound	R	Antibacterial Activity (Zone of inhibition in mm) <sup>a</sup>					
		S.aureus <sup>b</sup>	B.subtilis <sup>b</sup>	E.coli <sup>b</sup>	P.aeruginosa <sup>b</sup>	A.niger <sup>c</sup>	C.albicans <sup>c</sup>
TQVI(1)	H-	09	8	16	12	06	08
TQVI(2)	4-Cl-	16	17	16	20	07	12
TQVI(3)	3-NO <sub>2</sub> -	10	06	08	10	11	06
TQVI(4)	4-OH-	13	8	18	11	16	15
TQVI(5)	4-OCH <sub>3</sub> -	18	21	21	24	17	11

TQVI(6)	3,4,5-(OCH <sub>3</sub> ) <sub>3</sub> -	17	22	20	23	16	13
TQVI(7)	3,4-(OCH <sub>3</sub> ) <sub>2</sub> -	18	12	16	23	14	12
TQVI(8)	4-F-	18	15	19	20	08	14
TQVI(9)	4-CH <sub>2</sub> CH <sub>3</sub>	13	09	12	08	15	07
TQVI(10)	4-CH(CH <sub>3</sub> ) <sub>2</sub>	12	9	18	17	16	15
DMF <sup>d</sup>	-	-	-	-	-	-	-
Ampicillin	-	37	31	32	30		
Amphotericin B	-	-	-	-	-	18	17

<sup>a</sup> Zone of inhibition in mm : Zone of inhibition of microbial growth around the cups in the agar medium, measured in mm. <sup>b</sup> Bacteria tested: Staphylococcus aureus (MTCC 3160) and Bacillus subtilis (MTCC 441). Escherichia coli (MTCC 443) and Pseudomonas aeruginosa (MTCC 424).

<sup>c</sup> Fungi tested : Aspergillus niger (MTCC 282) and Candida albicans (MTCC 227)

<sup>d</sup> DMF: Dimethyl formamide.