3.1 Introduction

This chapter covers preparation and biological evaluation of novel 7-substituted tetrazolo[1,5-a]quinoline incorporated 1,3,4-oxadiazole compounds. The titled derivatives were synthesized by cyclization of variously substituted Schiff base analogues. Schiff base analogues were obtained by reaction between tetrazolo quinoline carbaldehyde with corresponding substituted benzyldrazide and nicotinohydrazide/isonicotinohydrazide. 1,3,4-oxadiazoles were obtained by cyclization of corresponding Schiff base analogues with different cyclizing reagents, among which (diacetoxyiodo)benzene was established to be an extremely good reagent. The compounds were prepared in good yield. $^1$H NMR, $^{13}$C NMR, IR and mass spectrometric techniques were employed to characterize the synthesized compounds. The synthesized compounds were screened for in vitro antioxidant, antibacterial, antimalarial and antitubercular potency. Many members of this novel 1,3,4-oxadiazole derivatives exhibited evident potencies as reference to standard drugs.

3.2 Literature survey on 1,3,4-oxadiazole derivatives

M. Pattarawarapan et al. reported[1] single pot preparation of 5-substituted 2-ethoxy-1,3,4-oxadiazoles under ultrasonication using N-acylbenzotriazoles and triphenyl-phosphine iodide. Various spectroscopic methods were used for characterization of synthesized compounds (Scheme 3.1).

L. Santhosh and his team[2] synthesized novel 2-amino-1,3,4-oxadiazole derivatives using cyclodeselenization approach using molecular-iodine. The titled compounds
were prepared from amino acid hydrazides (Nα-protected) and isoselenocyanato esters. The in situ formation of selenosemicarbazide intermediates led to the simplistic preparation of titled compounds in tremendous yield under mild conditions. This process is an environmentally green protocol employing iodine as the cyclizing agent and thereby avoiding the harsh conditions (Scheme 3.2).

**Scheme 3.2 Synthesis of Boc/Cbz-protected 2-amino-1,3,4-oxadiazole tethered peptidomimetics**

G. Ladani and Manish Patel reported[3] regioselective synthesis of quinoline fused 1,2,4-triazolo derivatives using multicomponent reaction approach. For the reaction they used various catalyst but out of them l-proline was established to be efficient catalyst for the preparation of titled compound without formation of undesired product. The synthesized titled compounds were analyzed by various spectrometric methods (Scheme 3.3).

**Scheme 3.3 Regioselective synthesis of substituted 1,2,4-triazolo[1,5-a]quinoline**
M. Basavanag et al. [4] synthesized tetrazolo[1,5-α]quinoline based 3-Imidazo[1,2-α]pyridine and 3-Tetrazolyl derivatives by using ring-chain and azido-tautomerization process under ultrasound or microwave irradiation. Various spectroscopic techniques were used for characterization of synthesized compounds (Scheme 3.4).

Huanfeng Jiang and his team [5] prepared 1,3,4-Oxadiazole-2(3H)-ones derivatives via oxidative carbonylation approach using palladium based catalyst (Scheme 3.5). Ramazani and Razaei [6] prepared 2,5-disubstituted-1,3,4-oxadiazoles using secondary amine, (N-isocyanimino)triphenylphosphorane, an aromatic aldehyde along with carboxylic acid in dichloromethane at very low temperature without catalyst (Scheme 3.6).
Xiuhai Gan and his group[7] reported preparation of 1,3,4-oxadiazole/thiadiazole chalcone analogues. The prepared compounds were evaluated for *in vitro* antiviral potencies using microscale thermophoresis and *in vivo* antiviral potency via half-leaf method (Figure 3.1).

**Figure 3.1** 1,3,4-oxadiazole/thiadiazole-chalcone conjugates

M. S. Shingare and his team[8] prepared novel tetrazolo[1,5-α]quinoline based α-acetoxyphosphonate and α-hydroxyphosphonate derivatives.

**Scheme 3.7** Synthesis of novel α-hydroxyphosphonates and α-acetoxyphosphonates
Compounds were tested for in vitro antifungal and antibacterial activity. The characterization of the prepared compounds was established by spectroscopic methods (Scheme 3.7).

M. E. Shoman et al.[9] reported preparation of novel 1,3,4-oxadiazole/oxime analogues. Synthesized compounds were evaluated for in vitro anti-inflammatory, COX inhibitory activity and ulcerogenic liability (Figure 3.2).

![Figure 3.2](image-url) 2-(5-phenyl-1,3,4-oxadiazole-2-thio)-1-phenylethanone oximes as anti-inflammatory agents

S. T. Dhumal and his team[10] prepared 1,3,4-oxadiazole based derivatives having pyridyl and thiazolyl groups using corresponding acid hydrazide and carboxylic acid derivatives in the presence of phosphorous oxychloride. Synthesized compounds were evaluated for in vitro antituberculosis potency against Mycobacterium bovis and Mycobacterium tuberculosis (MTB) (Scheme 3.8).

![Scheme 3.8](image-url) Synthesis of 2-pyridinyl substituted thiazolyl-5-aryl-1,3,4-oxadiazoles

S. S. Bharadwaj and his team[11] prepared 2,5-(disubstituted-[1,3,4])-oxadiazoles by cyclization of corresponding quinoline based Schiff base analogues. The compounds were tested for antimicrobial and antioxidant potentials (Scheme 3.9).
W. Gu et al. [12] developed quinoline and 1,3,4-oxadiazole derivatives from ursolic acid to check their anticancer as well in vitro cytotoxicity potency against Hela cancer cell lines. The structures of compounds were established by various spectroscopic methods (Figure 3.3).

![Scheme 3.9](image)

Scheme 3.9 Synthetic route for the synthesis of disubstituted-1,3,4-oxadiazoles

3.3 Present work

Profound interest has been observed for the preparation of heterocyclic motif because of unique pharmacological activities. Five-membered heterocyclic rings having oxygen, sulphur and nitrogen have broad spectrum of biological potencies. Therefore 2,5-disubstituted 1,3,4-oxadiazoles and 1,3,4-thiadiazoles have been chosen as a versatile moiety to synthesize compound of therapeutic significance[13-
19]. About 33% of the people are infected by *Mycobacterium tuberculosis* every year and more than 20 lakh deaths are reported over the globe[20]. Therefore TB has caused serious global issue related to health. World Health Organization has declared tuberculosis as ‘global emergency’ in recent assessment and showed that within the next 18-20 years around 3 crore people will be infected by *M. tuberculosis*[21-23]. The new forms of tuberculosis like MDR TB (multidrug resistant tuberculosis) and XDR TB (extensively drug resistant tuberculosis) are found to be rising as new challenge for medicinal chemists [24].

Similarly malaria has remained a noteworthy health problem with monetary and community consequences. Malaria is also dangerous disease around the globe. The occurrence of malaria is due to *Plasmodium falciparum* in most of the critical cases[25]. Quinoline clubbed antimalarial drugs such as chloroquine, amodiaquine, quinine, primaquine and mefloquine are prescribed for chemotherapy purpose[26-28].

Quinoline and its derivatives represent an imperative cluster of heterocyclic molecules occurring naturally as well as synthetically. They have pivotal applications in many biologically active products as well as various pharmacologically exciting compounds[29-32]. Azoles especially oxadiazoles and thiadiazole are gaining importance because of versatile property of liphophilicity. This can influence the capability of drug to reach the target through trans-membrane diffusion[33]. Quinoline clubbed 1,3,4-Oxadiazoles and 1,2,4-Oxadiazoles have exhibited broad range of pharmacological activities including antitubercular[34, 35], antibacterial [36, 37], antifungal[38, 39], antitumor[40, 41], antimalarial[42-45], and anti-inflammatory [46, 47] potencies and are key component of antibiotic furamizole[48] and antiretroviral raltegravil [49].

Keeping all these points in the mind, we planned and synthesized novel hybrid library of tetrazolo[1,5-a]quinoline clubbed 1,3,4-oxadiazoles having phenyl and pyridyl ring as the substituents in a single molecular framework with the expectation to acquire new molecules with enhanced antimycobacterial, antimalarial, antitubercular and antioxidant potencies.
3.4 Reaction scheme

The general reaction condition for the preparation of desired tetrazolo quinoline fused 1,3,4-oxadiazole scaffolds is elaborated in **Scheme 3.10**. 2-chloro-3-formylquinoline 1a-c was prepared via Vilsmeier-Haack reaction according to reported procedure[50]. 7-substituted tetrazolo[1,5-a]quinoline-4-carbaldehydes 3a-c were synthesized by reacting 7-substituted-2-chloro-3-formylquinoline 1 and sodium azide 2 using catalytic amount of acetic acid (glacial) and ethanol as solvent. 3a-c were refluxed with substituted benzohydrazide 4a-e/ nicotinohydrazide 4a'/isonicotinohydrazide 4b' in the presence of catalytic amount of glacial acetic acid in methanol for an hour to give (E)-4-substituted-N'-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)methylene)benzohydrazide 5a-l and (E)-N'-(7-substituted tetrazolo[1,5-a]quinolin-4-yl)methylene)nicotinohydrazide/isonicotinohydrazide 5m-r respectively. The obtained hydrazides *i.e.* 5a-l and 5m-r, were then subjected to an oxidative cyclization using (diacetoxyiodo)benzene (PhI(OAc)₂) in dichloromethane (DCM) for 20 min under stirring at room temperature to afford corresponding 1,3,4-
oxadiazoles derivatives *i.e.* 6a-l and 6m-r respectively. The cyclization of the resultant Schiff bases *i.e.* 5a-l and 5m-r was performed under different cyclizing reagents such as concentrated sulphuric acid, chloramine-T, mercuric acetate, lead dioxide, (diacetoxyiodo)benzene and aqueous sodium hydroxide with iodine in aqueous potassium iodide for comparison (*Table 3.1*).

### 3.5 Optimization of synthetic protocol

*Table 3.1* The influence of different cyclising reagents on the model reaction under different conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Time (min.)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Conc. H₂SO₄</td>
<td>Acetic acid</td>
<td>50</td>
<td>Trace</td>
</tr>
<tr>
<td>2</td>
<td>Chloramine-T</td>
<td>DCM</td>
<td>50</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>Hg(OAc)₂</td>
<td>Methanol</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>Hg(OAc)₂</td>
<td>DCM</td>
<td>35</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>IBD</td>
<td>DCM</td>
<td><strong>20</strong></td>
<td><strong>93</strong></td>
</tr>
<tr>
<td>6</td>
<td>IBD</td>
<td>Methanol</td>
<td>25</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>IBD</td>
<td>Ethanol</td>
<td>45</td>
<td>57</td>
</tr>
<tr>
<td>8</td>
<td>Aq. NaOH</td>
<td>Methanol</td>
<td>35</td>
<td>47</td>
</tr>
<tr>
<td>9</td>
<td>Aq. NaOH</td>
<td>DCM</td>
<td>40</td>
<td>55</td>
</tr>
<tr>
<td>10</td>
<td>Aq. NaOH</td>
<td>Ethanol</td>
<td>43</td>
<td>51</td>
</tr>
</tbody>
</table>

*a* Reaction of Schiff base 5a (1.0 mmol) in the presence of (1.0 mmol) catalyst

*b* Reaction progress monitored by TLC

*c* Isolated yield.

For the testing of different cyclizing reagents, we selected a model reaction between *(E)-N’-(tetrazolo[1,5-a]quinolin-4-ylmethylene)benzohydrazide 5a and different cyclizing reagents listed in *table 3.1*. After cyclization, the corresponding benzohydrazide derivatives get converted into the resultant product *i.e.* 7-substituted tetrazolo [1,5-a]quinoline incorporated 1,3,4-oxadiazole 6a-r.

We began our examination with variously substituted Schiff bases. Various Schiff base derivatives *i.e.* *(E)-4-substituted-N’-(7-substitutedtetrazolo [1,5-a]quinolin-4-yl)methylene)benzohydrazides 5a-l and *(E)-N’-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)methylene)nicotinohydrazide/isonicotinohydrazides (5m-r) were obtained by mixing equimolar amounts of tetrazolo[1,5-a]quinoline-4-carbaldehyde with the corresponding substitutedbenzohydrazide / nicotinohydrazide / isonicotinohydrazide.
in good to excellent yield using acetic acid (glacial) as the catalyst and methanol as a solvent over a time duration of 0.5-1.0 hr.

A series of experiments were performed to optimize the reaction conditions choosing the model reaction of (E)-N’-(tetrazolo[1,5-\(\alpha\)]quinolin-4-yl)methylene)benzohydrazide (1.0 mmol) 5a and different cyclizing reagents (1.0 mmol) (Table 3.1) in the various reaction media.

In order to find out the best solvent, the model reaction was performed using four different solvents viz. acetic acid, ethanol, methanol and dichloromethane (DCM) for the preparation of 6a. To optimize the reaction conditions, initially the reaction in acetic acid in the presence of concentrated H\(_2\)SO\(_4\) as the cyclising reagent was performed to afford targeted product 6a in very trace amount (Table 3.1, entry 1). After investigation in search for a suitable pair of cyclising reagent and various solvent, IBD was observed to be more efficient than other catalysts such as chloramine-T, mercuric acetate, aq. NaOH. IBD in dichloromethane(DCM) was the superior reagent over the other (entry 5, Table 3.1).

IBD was chosen as the cyclizing reagent for the preparation of tetrazolo [1,5-\(\alpha\)]quinoline incorporated 1,3,4-oxadiazoles. The reaction was then carried out in single pot by stirring different schiff bases 5a-r in the presence of (diacetoxyiodo)benzene at room temperature in DCM as the solvent to produce the desired 7-substituted tetrazolo [1,5-\(\alpha\)]quinoline incorporated 1,3,4-oxadiazoles (6a-r).
3.6 Experimental procedure

3.6.1 Synthesis of 2-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)-5-(p-substituted)-1,3,4-oxadiazole (6a-l) and 2-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)-5-(pyridin-3/4-yl)-1,3,4-oxadiazole (6m-r).

Following are the steps for the preparation of title compounds 6a-l and 6m-r.

3.6.1.1 Procedure for the synthesis of 7-substituted tetrazolo[1,5-a]quinoline-4-carbaldehyde (3a-c).

2-Chloroquinoline-3-carbaldehyde 1 (1 mmol), sodium azide 2 (2 mmol), 0.75 equiv. amount of acetic acid were refluxed in 50mL round bottom flask equipped with a condenser using ethanol as solvent. After reaction completion as detected by TLC, the reaction mass was allowed to cool down to room temperature. The separated solid crude product was filtered. It was washed with ethanol to obtain pure yellowish-white 7-substituted tetrazolo[1,5-a]quinoline-4-carbaldehydes (3a-c), after crystallization from the hot chloroform.

3.6.1.2 Procedure for the synthesis of (E)-4-substituted-N’-((7-substituted tetrazolo[1,5-a]quinolin-4-yl)methylene)benzohydrazide (5a-l).

An equimolar mixture of 7-substituted tetrazolo[1,5-a]quinoline-4-carbaldehyde 3a-c (1 mmol) and 4-substitutedbenzohydrazide 4a-e (1 mmol) were refluxed for 0.5-1 hour using 0.5 equiv. amount of acetic acid and methanol. After reaction completion as noticed by TLC, reaction mass was stirred magnetically for further 10-15 min at room temperature. After cooling, the separated solid mass was filtered, washed with methanol, dried and was crystallized from hot ethanol to yield aromatic Schiff bases (5a-l).

3.6.1.3 Procedure for the synthesis of (E)-N’-((7-substitutedtetrazolo[1,5-a]quinolin-4-yl)methylene)nicotinohydrazide/isonicotinohydrazide (5m-r).

An equimolar mixture of 7-substituted tetrazolo[1,5-a]quinoline-4-carbaldehyde 3a-c (1 mmol) and nicotinohydrazide (4a’)/ isonicotinohydrazide (4b’) (1 mmol) were refluxed for 0.5-1 hour in the presence of 0.5 equiv. acetic acid and methanol. The reaction mass was magnetically stirred for further 10-15 min at room temperature after reaction completion as noticed by TLC. After cooling the separated solid mass
was filtered, washed with methanol, dried, and was crystallized from hot ethanol to yield corresponding aromatic Schiff bases (5m-r).

3.6.1.4 Procedure for the synthesis of 2-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)-5-(p-substituted)-1,3,4-oxadiazole (6a-l).

Compound 5a-l (1 mmol) was taken in appropriate amount of methylenedichloride (MDC) solvent and stirred at room temperature. (Diacetoxyiodo)benzene (PhI(OAc)_2) (1 mmol) was slowly added and stirring was continued for 20-30 min at room temperature. After reaction completion as noticed by TLC, the solvent was evaporated and the residual part was washed with diethyl ether, filtered, dried and then crystallized from acetone to afford Schiff’s base corresponding 1,3,4-oxadiazole compounds (6a-l).

3.6.1.5 General procedure for the synthesis of 2-(7-substitutedtetrazolo[1,5-a]quinolin-4-yl)-5-(pyridin-3/4-yl)-1,3,4-oxadiazole (6m-r).

Compound 5m-r (1 mmol) was taken in appropriate amount of methylenedichloride (MDC) solvent and subjected to stirred at room temperature. To this stirred solution, (Diacetoxyiodo)benzene (PhI(OAc)_2) (1 mmol) was slowly added and the mass was stirred further for 20-30 min at room temperature. After completion of reaction as noticed by TLC, the solvent was evaporated and the residual part was washed with diethyl ether, filtered, dried and then crystallized from acetone to afford Schiff’s base corresponding pyridyl substituted 1,3,4-oxadiazole compounds (6m-r).
3.7 Preliminary-Spectral Characterizations

$^1$H NMR, $^{13}$C NMR, FT-IR, mass spectrometry and elemental analysis were employed to establish the structures of synthesized compounds. The IR spectrum of all the compounds had absorption near 1288-1220 cm$^{-1}$ due to aromatic C=N stretching. The characteristic C–H stretching of aromatic ring was observed at around 3069-3034 cm$^{-1}$. In $^1$H NMR spectra of the resultant compounds, the aromatic protons of quinoline and benzene resonate as multiplet around $\delta$ 7.45–9.31 ppm. The methyl and methoxy protons of the quinoline and benzene ring appeared near to $\delta$ 2.33 ppm and $\delta$ 3.91 ppm respectively. In $^{13}$C NMR spectra of the 1,3,4-oxadiazole ring, C-2 carbon was displayed as a very downfield signal at $\delta$ 164.1–165.9 ppm for the reason that it was in between one oxygen and one nitrogen atoms. The respective
chemical skeletons of all the compounds were confirmed by mass spectra showing molecular ion peaks (Base peak) corresponding to their molecular weights.

- All the synthesized compounds *i.e.* 6a-l and 6m-r are characterized by following spectral data.
### 2-phenyl-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

**Molecular Formula** \( \text{C}_{17} \text{H}_{10} \text{N}_{6} \text{O} \)  
**Molecular Weight (gm.mol\(^{-1}\))** 314.3  
**Melting Point (°C)** 214-216

**FT-IR** \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3059, 3034, 1606, 1540, 1222, 1088, 775, 715, 694

**\(^1\)H NMR** (δ ppm, DMSO-\(d_6\)): 7.57-8.75 (m, 9H, Ar-H), 9.30 (s, 1H, Ar-H)

**\(^{12}\)C NMR** (δ ppm, DMSO-\(d_6\)): 116.7, 126.9, 127.5, 128.4, 128.8, 128.9, 129.3, 130.1, 130.7, 132.9, 135.2, 146.0, 149.2, 164.1

**Elemental Analysis**  
Actual: C, 64.96%; H, 3.21%; N, 26.74%  
Found: C, 64.93%; H, 3.25%; N, 26.77%

### 2-(tetrazolo[1,5-a]quinolin-4-yl)-5-(p-tolyl)-1,3,4-oxadiazole

**Molecular Formula** \( \text{C}_{18} \text{H}_{12} \text{N}_{6} \text{O} \)  
**Molecular Weight (gm.mol\(^{-1}\))** 328.3  
**Melting Point (°C)** 207-209

**FT-IR** \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3057, 2919, 1609, 1539, 1496, 1085, 825, 775, 726

**\(^1\)H NMR** (δ ppm, DMSO-\(d_6\)): 2.46 (s, 3H, -CH\(_3\) of benzene ring), 7.51-8.74 (m, 8H, Ar-H), 9.27 (s, 1H, Ar-H)

**\(^{13}\)C NMR** (δ ppm, DMSO-\(d_6\)): 21.2, 116.7, 126.4, 127.1, 127.7, 128.6, 128.8, 130.3, 131.9, 136.0, 142.5, 146.4, 149.8, 165.6, 165.7

**Elemental Analysis**  
Actual: C, 65.65%; H, 3.68%; N, 25.60%  
Found: C, 65.82%; H, 3.66%; N, 25.64%
2-(4-methoxyphenyl)-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

Molecular Formula: C_{18}H_{12}N_{6}O_{2}
Molecular Weight (g/mol): 344.3
Melting Point (°C): 195-197

FT-IR: \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3058, 2920, 1610, 1538, 1498, 1239, 1086, 824, 775

\(^1\)H NMR (δ ppm, DMSO-\(d_6\)): 3.91 (s, 3H, -OCH\(_3\) of benzene ring), 7.57 - 8.74 (m, 8H, Ar-H), 9.26 (s, 1H, Ar-H)

\(^13\)C NMR (δ ppm, DMSO-\(d_6\)): 54.2, 114.3, 115.5, 116.0, 126.8, 127.5, 128.7, 129.0, 129.8, 130.8, 135.6, 146.0, 149.8, 160.3, 165.2

Elemental Analysis
Actual: C, 62.79; H, 3.51; N, 24.41%
Found: C, 62.77; H, 3.49; N, 24.43%

---

2-(4-chlorophenyl)-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

Molecular Formula: C\(_{17}\)H\(_6\)ClN\(_6\)O
Molecular Weight (g/mol): 348.7
Melting Point (°C): 196-198

FT-IR: \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3060, 3033, 1607, 1539, 1220, 1089, 776, 713, 693

\(^1\)H NMR (δ ppm, DMSO-\(d_6\)): 7.53 - 8.75 (m, 8H, Ar-H), 9.21 (s, 1H, Ar-H)

\(^13\)C NMR (δ ppm, DMSO-\(d_6\)): 116.7, 124.6, 127.3, 128.5, 128.8, 128.9, 129.2, 130.1, 130.7, 134.3, 135.3, 145.8, 149.7, 164.9

Elemental Analysis
Actual: C, 58.55; H, 2.60; N, 24.10%
Found: C, 58.57; H, 2.61; N, 24.14%
2-(4-bromophenyl)-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

- Molecular Formula: C_{17}H_{15}BrN_{6}O
- Molecular Weight (g.mol^{-1}): 393.2
- Melting Point (°C): 191-193

FT-IR: \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3061, 3034, 1606, 1541, 1221, 1085, 775, 712, 690

\(^1\)H NMR (δ ppm, DMSO-d_6): 7.52 - 9.18 (m, 9H, Ar-H)

\(^13\)C NMR (δ ppm, DMSO-d_6): 116.7, 123.3, 125.7, 126.0, 128.1, 128.5, 129.2, 129.8, 130.7, 132.7, 135.6, 145.4, 149.7, 165.9

Elemental Analysis: Actual: C, 51.93; H, 2.31; N, 21.37%
Found: C, 51.91; H, 2.29; N, 21.34%

2-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-5-phenyl-1,3,4-oxadiazole

- Molecular Formula: C_{18}H_{15}N_{6}O
- Molecular Weight (g.mol^{-1}): 328.3
- Melting Point (°C): 200-202

FT-IR: \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3058, 2920, 1610, 1539, 1495, 1086, 824, 773, 722

\(^1\)H NMR (δ ppm, DMSO-d_6): 2.33 (s, 3H, -CH_3 of quinoline ring), 7.55 - 8.75 (m, 8H, Ar-H), 9.31 (s, 1H, Ar-H)

\(^13\)C NMR (δ ppm, DMSO-d_6): 21.5, 126.9, 127.1, 128.4, 128.6, 129.5, 131.5, 130.0, 130.9, 133.6, 134.7, 136.3, 141.7, 149.7, 164.8

Elemental Analysis: Actual: C, 58.55; H, 2.60; N, 24.10%
Found: C, 58.57; H, 2.61; N, 24.14%
2-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-5-(p-tolyl)
-1,3,4-oxadiazole

Molecular Formula $C_{19}H_{14}N_5O$
Molecular Weight (gm.mol$^{-1}$) 342.3
Melting Point (°C) 197-199

FT-IR $\nu_{max}$ cm$^{-1}$ (KBr): 3056, 2919, 1610, 1540, 1495, 1089, 826, 774, 723

$^1$H NMR (δ ppm, DMSO-$d_6$): 2.33 (s, 3H, -CH$_3$ of quinoline ring), 2.67 (s, 3H, -CH$_3$ of benzene ring), 7.54 -8.64 (m, 7H, Ar-H), 9.19 (s, 1H, Ar-H)

$^{13}$C NMR (δ ppm, DMSO-$d_6$): 21.4, 21.9, 126.4, 127.5, 127.9, 128.0, 128.9, 130.2, 131.3, 131.9, 134.0, 136.8, 142.8, 144.1, 149.3, 164.9

Elemental Analysis Actual: C, 66.66; H, 4.12; N, 24.55%
Found: C, 66.63; H, 4.14; N, 24.53%

2-(4-methoxyphenyl)-5-(7-methyltetrazolo[1,5-a]quinolin-4-yl)
-1,3,4-oxadiazole

Molecular Formula $C_{19}H_{14}N_5O_2$
Molecular Weight (gm.mol$^{-1}$) 358.3
Melting Point (°C) 201-203

FT-IR $\nu_{max}$ cm$^{-1}$ (KBr): 3057, 2919, 1611, 1540, 1238, 1085, 826, 775, 721

$^1$H NMR (δ ppm, DMSO-$d_6$): 2.33 (s, 3H, -CH$_3$ of quinoline ring), 3.92 (s, 3H, -OCH$_3$ of benzene ring), 7.53 -9.22 (m, 8H, Ar-H)

$^{13}$C NMR (δ ppm, DMSO-$d_6$): 21.8, 55.9, 114.3, 115.8, 126.7, 128.5, 128.9, 130.4, 131.8, 134.6, 136.8, 144.0, 148.6, 160.3, 165.5

Elemental Analysis Actual: C, 63.68; H, 3.94; N, 23.45%
Found: C, 63.66; H, 3.96; N, 23.47%
### Tetrazolo[1,5-α]quinoline based 1,3,4-oxadiazole

#### 2-(4-chlorophenyl)-5-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

**Molecular Formula**  \( \text{C}_{18}\text{H}_{17}\text{ClN}_{6}\text{O} \)

**Molecular Weight (gm.mol\(^{-1}\))** 362.7

**Melting Point (°C)** 204-206

**FT-IR**  \( \nu_{\text{max}} \text{ cm}^{-1} (\text{KBr}) \): 3060, 3031, 1609, 1539, 1235, 1051, 779, 714, 693

\(^1\text{H} \text{NMR} (\delta \text{ ppm, DMSO-}d_6): 2.33 \text{ (s, 3H, -CH}_3\text{ of quinoline ring)}, 7.55 - 9.23 \text{ (m, 8H, Ar-H)}

\(^13\text{C} \text{NMR} (\delta \text{ ppm, DMSO-}d_6): 21.7, 124.3, 126.9, 128.4, 128.7, 128.9, 129.8, 130.5, 131.7, 134.6, 135.1, 136.7, 143.8, 148.9, 165.7

**Elemental Analysis**  Actual: C, 59.59; H, 3.06; N, 23.17%

Found: C, 59.60; H, 3.09; N, 23.18%

---

#### 2-(7-methoxytetrazolo[1,5-a]quinolin-4-yl)-5-phenyl-1,3,4-oxadiazole

**Molecular Formula**  \( \text{C}_{18}\text{H}_{12}\text{N}_{6}\text{O}_2 \)

**Molecular Weight (gm.mol\(^{-1}\))** 344.3

**Melting Point (°C)** 220-222

**FT-IR**  \( \nu_{\text{max}} \text{ cm}^{-1} (\text{KBr}) \): 3059, 3032, 1607, 1538, 1236, 1083, 821, 778, 722

\(^1\text{H} \text{NMR} (\delta \text{ ppm, DMSO-}d_6): 3.90 \text{ (s, 3H, -OCH}_3\text{ of quinoline ring)}, 7.56 - 8.73 \text{ (m, 8H, Ar-H)}, 9.27 \text{ (s, 1H, Ar-H)}

\(^13\text{C} \text{NMR} (\delta \text{ ppm, DMSO-}d_6): 55.4, 103.9, 120.0, 127.5, 127.8, 129.2, 129.5, 130.9, 131.2, 133.6, 133.9, 141.7, 146.8, 157.1, 165.2

**Elemental Analysis**  Actual: C, 62.79; H, 3.51; N, 24.41%

Found: C, 62.77; H, 3.49; N, 24.43%
2-(7-methoxytetrazolo[1,5-a]quinolin-4-yl)-5-(p-tolyl) -1,3,4-oxadiazole

Molecular Formula: C_{19}H_{14}N_{6}O_{3}
Molecular Weight (gm.mol⁻¹): 374.3
Melting Point (°C): 208-210

FT-IR: ν_{max} cm⁻¹ (KBr): 3057, 2918, 1609, 1540, 1413, 1239, 828, 775, 722

¹H NMR (δ ppm, DMSO-d₆): 3.89 (s, 3H, -OCH₃ of benzene ring), 3.98 (s, 3H, -OCH₃ of quinoline ring), 7.54 - 9.23 (m, 8H, Ar-H)

¹³C NMR (δ ppm, DMSO-d₆): 55.6, 55.9, 105.8, 114.8, 115.3, 122.7, 129.1, 129.8, 130.7, 131.5, 134.6, 141.8, 147.3, 157.4, 160.7, 165.2

Elemental Analysis: Actual: C, 60.96; H, 3.77; N, 22.45%
Found: C, 60.99; H, 3.78; N, 22.43%
2-(pyridin-4-yl)-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

Molecular Formula \( \text{C}_{16}\text{H}_{13}\text{N}_{7}\text{O} \)
Molecular Weight (gm.mol\(^{-1}\)) 315.2
Melting Point (\(^{\circ}\)C) 201-203

FT-IR \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3034, 1609, 1572, 1414, 1372, 1282, 1128, 785, 685

\(^1\)H NMR (\(\delta\) ppm, DMSO-\(d_6\)): 7.85 - 8.80 (m, 9H, Ar-H)

\(^{13}\)C NMR (\(\delta\) ppm, DMSO-\(d_6\)): 116.7, 122.1, 124.3, 128.9, 130.6, 131.0, 132.6, 144.8, 147.7, 150.2, 164.1, 165.5

Elemental Analysis
Actual: C, 60.95; H, 2.88; N, 31.10%
Found: C, 60.92; H, 2.87; N, 31.11%

2-(pyridin-3-yl)-5-(tetrazolo[1,5-a]quinolin-4-yl)-1,3,4-oxadiazole

Molecular Formula \( \text{C}_{16}\text{H}_{13}\text{N}_{7}\text{O} \)
Molecular Weight (gm.mol\(^{-1}\)) 315.2
Melting Point (\(^{\circ}\)C) 211-213

FT-IR \( \nu_{\text{max}} \text{ cm}^{-1} \) (KBr): 3034, 1609, 1572, 1414, 1372, 1282, 1128, 785, 685

\(^1\)H NMR (\(\delta\) ppm, DMSO-\(d_6\)): 7.85 - 8.80 (m, 9H, Ar-H)

\(^{13}\)C NMR (\(\delta\) ppm, DMSO-\(d_6\)): 116.7, 122.1, 124.3, 128.9, 130.6, 131.0, 132.6, 144.8, 147.7, 150.2, 164.1, 165.5

Elemental Analysis
Actual: C, 60.95; H, 2.88; N, 31.10%
Found: C, 60.93; H, 2.89; N, 31.09%
Tetrazolo[1,5-a]quinoline based 1,3,4-oxadiazole

2-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazole

Molecular Formula: C_{17}H_{11}N_{3}O
Molecular Weight (gm.mol^{-1}): 329.3
Melting Point (°C): 207-209

FT-IR: $\nu_{\text{max}} \text{ cm}^{-1} (\text{KBr})$: 30.5, 1609, 1573, 1413, 1376, 1286, 1127, 782, 686

$^1$H NMR (δ ppm, DMSO-$d_6$): 2.55 (s, 3H, -CH$_3$ of quinoline ring), 7.77 - 8.96 (m, 8H, Ar-H)

$^{13}$C NMR (δ ppm, DMSO-$d_6$): 21.5, 121.1, 126.9, 127.9, 128.4, 130.7, 131.2, 134.4, 136.9, 143.2, 143.7, 148.6, 149.9, 164.8

Elemental Analysis
Actual: C, 62.00; H, 3.37; N, 29.77%
Found: C, 62.04; H, 3.40; N, 29.75%

2-(7-methyltetrazolo[1,5-a]quinolin-4-yl)-5-(pyridin-3-yl)-1,3,4-oxadiazole

Molecular Formula: C_{17}H_{11}N_{3}O
Molecular Weight (gm.mol^{-1}): 329.3
Melting Point (°C): 208-210

FT-IR: $\nu_{\text{max}} \text{ cm}^{-1} (\text{KBr})$: 3036, 1610, 1572, 1412, 1375, 1288, 1128, 786, 683

$^1$H NMR (δ ppm, DMSO-$d_6$): 2.55 (s, 3H, -CH$_3$ of quinoline ring), 7.75 - 8.04 (m, 8H, Ar-H)

$^{13}$C NMR (δ ppm, DMSO-$d_6$): 21.8, 124.0, 124.7, 126.8, 128.4, 128.9, 130.8, 131.6, 134.0, 134.8, 136.7, 144.1, 147.3, 148.8, 152.5, 165.6

Elemental Analysis
Actual: C, 60.95; H, 2.88; N, 31.10%
Found: C, 60.93; H, 2.89; N, 31.09%
<table>
<thead>
<tr>
<th>Molecular Formula</th>
<th>C&lt;sub&gt;17&lt;/sub&gt;H&lt;sub&gt;12&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Molecular Weight (g/mol)</th>
<th>345.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting Point (°C)</td>
<td>197-199</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FT-IR** \( \nu_{\text{max}} \text{ cm}^{-1} (\text{KBr}) \): 3069, 2992, 1590, 1477, 1413, 1362, 1247, 1041, 858, 846, 652

**\(^1\)H NMR** (δ ppm, DMSO-\(d_6\)): 3.90 (s, 3H, \text{-OCH}_3 \text{ of quinoline ring}), 7.45 - 8.48 (m, 7H, Ar-H), 8.76 (s, 1H, Ar-H)

**\(^13\)C NMR** (δ ppm, DMSO-\(d_6\)): 55.7, 105.5, 121.8, 122.9, 130.1, 131.8, 134.6, 141.5, 143.8, 147.7, 150.0, 157.8, 164.9

**Elemental Analysis**

Actual: C, 59.13; H, 3.21; N, 28.39%

Found: C, 59.10; H, 3.18; N, 28.38%
Figure 3.4 Mass spectrum of compound 6a

Figure 3.5 FT-IR spectrum of compound 6a
Tetrazolo[1,5-a]quinoline based 1,3,4-oxadiazole

Figure 3.6 $^1$H NMR spectrum of compound 6a

Figure 3.7 APT spectrum of compound 6a
Figure 3.8 Mass spectrum of compound 6b

Figure 3.9 FT-IR spectrum of compound 6b
Tetrazolo[1,5-a]quinoline based 1,3,4-oxadiazole

Figure 3.10 $^1$H NMR spectrum of compound 6b

Figure 3.11 APT spectrum of compound 6b
Figure 3.12 Mass spectrum of compound 6m

Figure 3.13 FT-IR spectrum of compound 6m
Tetrazolo[1,5-a]quinoline based 1,3,4-oxadiazole

Figure 3.14 $^1$H NMR spectrum of compound 6m

Figure 3.15 APT spectrum of compound 6m
Figure 3.16 Mass spectrum of compound 6q

Figure 3.17 FT-IR spectrum of compound 6q
Figure 3.18 $^1$H NMR spectrum of compound 6q

Figure 3.19 APT spectrum of compound 6q
3.8 Biological study

The synthesized titled compounds were further tested for *in vitro* antimalarial, antioxidant, antituberculosis and antimicrobial potencies. The detailed data are as follows.

### 3.8.1 Antibacterial activity

**Table 3.3** *In vitro* antimicrobial activity expressed in terms of MIC, µg/mL for prepared derivatives 6a-l and 6m-r.

<table>
<thead>
<tr>
<th>Comp. code</th>
<th>Gram positive bacteria</th>
<th>Gram negative bacteria</th>
<th>Fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S.P.</td>
<td>B.S.</td>
<td>C.T.</td>
</tr>
<tr>
<td>1936</td>
<td>441</td>
<td>449</td>
<td>443</td>
</tr>
<tr>
<td>6a</td>
<td>500</td>
<td>200</td>
<td>500</td>
</tr>
<tr>
<td>6b</td>
<td>100</td>
<td>500</td>
<td>250</td>
</tr>
<tr>
<td>6c</td>
<td>100</td>
<td>200</td>
<td>500</td>
</tr>
<tr>
<td>6d</td>
<td>62.5</td>
<td>500</td>
<td>1000</td>
</tr>
<tr>
<td>6e</td>
<td>500</td>
<td>250</td>
<td>500</td>
</tr>
<tr>
<td>6f</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>6g</td>
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<td>500</td>
<td>500</td>
</tr>
<tr>
<td>6h</td>
<td>250</td>
<td>200</td>
<td>100</td>
</tr>
<tr>
<td>6i</td>
<td>200</td>
<td>100</td>
<td>62.5</td>
</tr>
<tr>
<td>6j</td>
<td>500</td>
<td>500</td>
<td>250</td>
</tr>
<tr>
<td>6k</td>
<td>100</td>
<td>1000</td>
<td>100</td>
</tr>
<tr>
<td>6l</td>
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<td>500</td>
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<tr>
<td>6m</td>
<td>200</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>6n</td>
<td>500</td>
<td>62.5</td>
<td>500</td>
</tr>
<tr>
<td>6o</td>
<td>100</td>
<td>1000</td>
<td>62.5</td>
</tr>
<tr>
<td>6p</td>
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<td>200</td>
<td>500</td>
</tr>
<tr>
<td>6q</td>
<td>100</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>6r</td>
<td>62.5</td>
<td>1000</td>
<td>100</td>
</tr>
<tr>
<td>A</td>
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<td>100</td>
<td>50</td>
</tr>
<tr>
<td>C</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>D</td>
<td>25</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>E</td>
<td>n. t.</td>
<td>n. t.</td>
<td>n. t.</td>
</tr>
<tr>
<td>F</td>
<td>n. t.</td>
<td>n. t.</td>
<td>n. t.</td>
</tr>
</tbody>
</table>


The titled compounds 6a-l and 6m-r were screened for *in vitro* antimicrobial activity using three gram +ve and three gram -ve bacteria using standard drugs according to NCCLS (National Committee for Clinical Laboratory Standards)[51]. The antimicrobial screening result data is mentioned in Table 3.3.

**Table 3.3** summarizes the test results of all prepared compounds. The majority of the synthesized compounds showed good resistance against bacteria.
with reference to at least one of the standard drugs i.e. ampicillin, norfloxacin or ciprofloxacin. It is marked that in screening of Gram positive species, against *S. pneumoniae*, compound 6d and 6r were noticed to be highly potent (i.e. 62.5 µg/mL) with reference to chloramphenicol (i.e. 50 µg/mL). Compounds 6c, 6b, 6g, 6j, 6k, 6o and 6q displayed similar MIC or somewhat lesser activity with reference to ampicillin (i.e. 100 µg/mL). Amongst prepared library, compound 6q showed maximum activity against five gram negative and positive bacterial species with reference to ampicillin, norfloxacin, chloramphenicol and ciprofloxacin. Compound 6n expressed excellent inhibition against *B. substilis* as compared chloramphenicol and also compounds 6a, 6c, 6d, 6e, 6g, 6h, 6i, 6m, 6q and 6p showed significant activity as standard drugs described above. Compounds 6h, 6k, 6m, 6o and 6r exposed equal MIC (i.e. 100 µg/mL) as ciprofloxacin against *C. tetani*. Compounds 6i, 6m and 6p revealed noteworthy activity against four gram negative and positive bacterial species. Many of those compounds expressed significant inhibitory power against three gram negative and positive bacterial species.

Gram negative bacterial screening observation shows that, compound 6p and 6f showed excellent resistance against *S. typhi* and *V. cholerae* respectively with reference to chloramphenicol. Compounds 6k, 6d, 6q and 6n are relatively more potent (i.e. 250 µg/mL) to griseofulvin and compounds 6e, 6h, 6i, and 6o expressed griseofulvin equivalent power (i.e. 500 µg/mL). The compounds from the prepared library did not show similar potency with reference to the standards against *A. Fumigatus*.

### 3.8.2 Fungicidal activity

The fungicidal activity data of the synthesized tetrazolo quinoline based oxadiazoles derivatives are presented in Table 3.3. Some of the prepared compounds exhibited good fungicidal activity particularly against *Candida albicans*. Compounds 6k, 6d, 6q and 6n are relatively more potent (i.e. 250 µg/mL) to griseofulvin and compounds 6e, 6h, 6i, and 6o expressed griseofulvin equivalent power (i.e. 500 µg/mL). The compounds from the prepared library did not show similar potency with reference to the standards against *A. Fumigatus*.
3.8.3 Antituberculosis activity

*In vitro* antiTB potency of the compounds 6a-l and 6m-r was carried out at two different concentrations (*i.e.* 250 and 100 μg/mL) against *M. tuberculosis* H37Rv strain by following the standard procedure described by A. Rattan[36] using standard drugs. The results in the form of % inhibition are mentioned in **Table 3.4**.

**Table 3.4** *In vitro* antituberculosis activity (% inhibition) of 1,3,4-oxadiazole derivatives 6a-l and 6m-r against *M. tuberculosis* H37Rv (at 250 and 100 μg/mL concentration level).

<table>
<thead>
<tr>
<th>Comp. code</th>
<th>% Inhibition 250 μg/mL</th>
<th>% Inhibition 100 μg/mL</th>
<th>Comp. code</th>
<th>% Inhibition 250 μg/mL</th>
<th>% Inhibition 100 μg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>65</td>
<td>31</td>
<td>6k</td>
<td>78</td>
<td>49</td>
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<tr>
<td>6b</td>
<td>79</td>
<td>54</td>
<td>6l</td>
<td>83</td>
<td>67</td>
</tr>
<tr>
<td>6c</td>
<td>35</td>
<td>12</td>
<td>6m</td>
<td>94</td>
<td>80</td>
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<tr>
<td>6d</td>
<td>92</td>
<td>79</td>
<td>6n</td>
<td>76</td>
<td>55</td>
</tr>
<tr>
<td>6e</td>
<td>64</td>
<td>43</td>
<td>6o</td>
<td>70</td>
<td>43</td>
</tr>
<tr>
<td>6f</td>
<td>48</td>
<td>23</td>
<td>6p</td>
<td>65</td>
<td>37</td>
</tr>
<tr>
<td>6g</td>
<td>53</td>
<td>29</td>
<td>6q</td>
<td>98</td>
<td>87</td>
</tr>
<tr>
<td>6h</td>
<td>95</td>
<td>77</td>
<td>6r</td>
<td>85</td>
<td>62</td>
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<tr>
<td>6i</td>
<td>86</td>
<td>63</td>
<td>Rifampicin</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>6j</td>
<td>71</td>
<td>51</td>
<td>Isoniazid</td>
<td>99</td>
<td>99</td>
</tr>
</tbody>
</table>

Antituberculosis evaluation of synthesized tetrazoloquinoline based 1,3,4-oxadiazoles 6a-r was performed at two concentrations *i.e.* 250 and 100 μg/mL against *M. tuberculosis* H37Rv strain. Preliminary screening shows that compound 6d, 6h, 6m and 6q had highest *M. Tuberculosis* H37Rv strain bacterial resistance with 90-100% growth inhibition at concentration level 250μg/mL.

The compounds 6i, 6l and 6r showed 80-90% growth inhibition at the same concentration level. The compounds showing higher growth inhibition power were further tested at concentration level 100μg/mL. Residual compounds did not show significant % growth inhibition in the test (Table 3.4).
3.8.4 Antimalarial activity

Table 3.5 *In vitro* antimalarial activity of 1,3,4-oxadiazole derivatives 6a-l and 6m-r.

<table>
<thead>
<tr>
<th>Comp. code</th>
<th>IC&lt;sub&gt;50&lt;/sub&gt; (µg/mL)</th>
<th>Comp. code</th>
<th>IC&lt;sub&gt;50&lt;/sub&gt; (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>0.066</td>
<td>6k</td>
<td>0.82</td>
</tr>
<tr>
<td>6b</td>
<td>1.23</td>
<td>6l</td>
<td>1.89</td>
</tr>
<tr>
<td>6c</td>
<td>1.55</td>
<td>6m</td>
<td>0.079</td>
</tr>
<tr>
<td>6d</td>
<td><strong>0.047</strong></td>
<td>6n</td>
<td>0.85</td>
</tr>
<tr>
<td>6e</td>
<td>0.41</td>
<td>6o</td>
<td>1.32</td>
</tr>
<tr>
<td>6f</td>
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<td>6p</td>
<td><strong>0.043</strong></td>
</tr>
<tr>
<td>6g</td>
<td>1.53</td>
<td>6q</td>
<td><strong>0.039</strong></td>
</tr>
<tr>
<td>6h</td>
<td><strong>0.059</strong></td>
<td>6r</td>
<td>0.37</td>
</tr>
<tr>
<td>6i</td>
<td>0.58</td>
<td>Chloroquine</td>
<td>0.020</td>
</tr>
<tr>
<td>6j</td>
<td>0.51</td>
<td>Quinine</td>
<td>0.268</td>
</tr>
</tbody>
</table>

Compounds 6a-l and 6m-r were screened for *in vitro* anti-malarial activity against *P. falciparum* strain using standard drugs. The screening results in the form of 50% inhibitory concentration (*i.e.* IC<sub>50</sub>) of the parasitic growth are mentioned in Table 3.5. Duplicate runs were performed for each experiment and average values of IC<sub>50</sub> are presented in Table 3.5. Compounds 6a, 6l, 6n, 6p and 6s had IC<sub>50</sub> in the range of 0.039 to 0.079 for the *P. falciparum* strain, which displayed better potency against *P. falciparum* strain with reference to quinine IC<sub>50</sub> 0.268. Residual compounds of the series were found to be less potent against *P. falciparum* with reference to the standard drugs.
3.8.5 Antioxidant activity

Table 3.6 *In vitro* antioxidant activity of compounds 6a-l and 6m-r.

<table>
<thead>
<tr>
<th>Comp. code</th>
<th>OD (593 nm)</th>
<th>FRAP value a</th>
<th>Comp. code</th>
<th>OD (593 nm)</th>
<th>FRAP value a</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
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<td>6k</td>
<td>0.721</td>
<td>145.48</td>
</tr>
<tr>
<td>6b</td>
<td>1.689</td>
<td>340.80</td>
<td>6l</td>
<td>1.103</td>
<td>222.56</td>
</tr>
<tr>
<td>6c</td>
<td>1.346</td>
<td>271.59</td>
<td>6m</td>
<td>2.312</td>
<td><strong>466.51</strong></td>
</tr>
<tr>
<td>6d</td>
<td><strong>2.135</strong></td>
<td><strong>430.80</strong></td>
<td>6n</td>
<td>1.701</td>
<td>343.22</td>
</tr>
<tr>
<td>6e</td>
<td>1.117</td>
<td>225.38</td>
<td>6o</td>
<td>1.415</td>
<td>285.51</td>
</tr>
<tr>
<td>6f</td>
<td>1.783</td>
<td>359.77</td>
<td>6p</td>
<td>1.714</td>
<td>345.85</td>
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<tr>
<td>6g</td>
<td>1.236</td>
<td>249.40</td>
<td>6q</td>
<td><strong>2.178</strong></td>
<td><strong>439.47</strong></td>
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<tr>
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<td>390.24</td>
<td>6r</td>
<td>1.697</td>
<td>342.42</td>
</tr>
<tr>
<td>6i</td>
<td>0.834</td>
<td>168.28</td>
<td>A.A.</td>
<td>2.501</td>
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</tr>
<tr>
<td>6j</td>
<td>1.273</td>
<td>256.86</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A.A. = ascorbic acid, concentration of compounds used = 200 mg/mL, concentration of standard (A.A.) = 176 mg/mL. a A.A. mmol per 100 gm of the sample. FRAP = ferric reducing antioxidant power

Upon investigation of the FRAP (ferric reducing antioxidant power), it is noticed that most of the prepared compounds showed FRAP values ranging from 466.51 to 63.35 mmol per 100gm of compounds. This indicates that the prepared compounds are better antioxidants. Amongst them compound 6m expressed remarkable antioxidant activity (Table 3.6).

3.9 Structure activity relationship (SAR)

The study of pharmacological screening is helpful to correlate the diverse potency of compounds and pattern of substitution on tetrazoloquinoline and benzene/pyridine. From the structure activity relationship, it is concluded that pyridine substituted ring shows the diversified importance to enhance the biological activity of the compounds in comparison to simple benzene ring (Figure 3.20).
3.10 Conclusion

This study presents preparation of 18 new quinoline-oxadiazole hybrids showing some remarkable biological results. This work helps to corroborate the choice of the quinoline fused 1,3,4-oxadiazole scaffold as a useful model for designing new antimicrobial, antitubercular, antimalarial and antioxidant agents. Two leading candidates (6h and 6q) displayed modest antituberculosis potency. Some of the candidates showed brilliant antimalarial activity against *P. falciparum* with reference to quinine. Compound 6q has come out as the promising antimicrobial member of the series, showing better antitubercular, antimalarial as well antioxidant potencies. The results point towards the fact that oxadiazoles scaffold which is clubbed with the pyridine ring exhibited the highest antibacterial, antituberculosis and antimalarial potency[52].
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