RESEARCH ARTICLE

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Synthesis and Comparison of Substituted Quinazolinone Analogs with Quinolones as Antitubercular and Antibacterial Agents

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Abstract
In recent years there has been a tremendous increase of drug resistant pathogens, especially *M. tuberculosis*, leading to the design and development of newer antimycobacterial compounds. The reaction of 3-amino-2-(2-chlorophenyl) quinazolin-4(3H)-one with various 2-chloro-N-(substituted phenyl)acetamide derivatives provided the target compounds. The structure of the compounds has been confirmed by IR, ^{1}H NMR and Mass spectral data. Antitubercular and antibacterial activities were performed by microbroth dilution and cup plate method respectively. The compounds have shown significant antitubercular and moderate antibacterial activity when compared with the standard drugs.

Keywords: Quinazolin-4(3*H*)-one; antitubercular and antibacterial activity.

1. Introduction

Review from the World Health Organization shows a significant rise in drug-resistant tuberculosis. Tuberculosis (TB) is one of the leading causes of death and suffering worldwide among the infectious diseases. The ever-increasing drug resistance, toxicity, side effects and the absence of their bactericidal activity highlight the need for new, safer and more effective anti-tubercular drugs [1]. Every year, approximately 8 million of infected people develop active TB, and almost 2 million of them die from the disease, a life is lost to TB every 15s. The incidence of TB infection has steadily risen in the last decade and this increase can be attributed to a similar increase in human immunodeficiency virus (HIV) infection. The association of TB and HIV infections is so dramatic that, in some cases, nearly two-thirds of the patients diagnosed with TB are also HIV-1 seropositive. Furthermore, numerous studies have shown that TB is a cofactor in the progression of HIV infection [2]. The re-emergence of TB infection has been further complicated by an increase in the prevalence of drug-resistant TB cases. Current control efforts are severely hampered due to *M. tuberculosis* being a leading opportunistic infection in patients with acquired immuno deficiency syndrome and the spreading of multidrug-resistant strains (MDR-MTB). Problems in the chemotherapy of tuberculosis arise when patients develop bacterial resistance to the first-line drugs: isoniazid, rifampicin, ethambutol, streptomycin and pyrazinamide.

The newer tuberculosis drugs which have shown promising results are Rifabutin [3], Ansamycin [4] and 4-quinolones, which is another group that has shown promising antimycobacterial activity in the recent past [5, 6]. A number of quinazolinone analogs have been synthesized and evaluated for antitubercular activity. Ofloxacin has been found to be very effective both *in vitro* [7, 8] against *M. tuberculosis* and has been proved to be quite safe. Another quinolone, Ciprofloxacin, has also shown encouraging *in vitro* activity [9]. Treatment outcomes of XDR-TB, which is MDR-TB with additional bacillary resistance to any second-line agent, are worse than those of MDR-TB [10]. Fluoroquinolones are important second-line antitubercular drugs. Besides being increasingly popular in treatment of TB complicated by intolerance of relative contraindication for first-line drugs, fluoroquinolones are important for improving treatment outcomes of MDR-TB [11, 12]. Newer fluoroquinolones such as moxifloxacin have demonstrated potential for shortening treatment duration [13-15] and has been recommended in treatment of XDR-TB [16].

2. Methods

Melting points were measured in open capillary tubes and are uncorrected. IR (KBR) spectra were recorded in film or in potassium bromide disks on a Perkin-Elmer 39 spectrophotometer (υ max in cm^{-1}) and ^{1}H NMR spectra on a DPX 300 MHz Bruker FT-NMR spectrophotometer. The chemical shifts were reported as parts per million (δ ppm) using tetramethyl silane (TMS) as internal standard. Mass spectra were obtained on a JEOL-SX-102 instrument

using fast atom bombardment (FAB positive). The progress of the reaction was monitored on a readymade silica gel plates (Merck) using n-hexane: ethyl acetate as a solvent system. Spectral data (UV, IR, ^{1}HNMR and Mass spectra) confirmed the structure of the synthesized compounds and the purity of these compounds were ascertained by microanalysis.

Procedure

Synthesis of 3-amino-2-(2-chlorophenyl)-quinazolin-4(3*H*)-one (i)
Anthranilic acid (1.37g, 0.01m) was taken in a beaker containing 30ml of distilled and dried pyridine, 2-chlorobenzoyl chloride (1.74g, 0.01m) was added slowly drop wise with stirring in cold condition. After the complete addition of 2-chlorobenzoyl chloride the reaction mixture was stirred for 4h at room temperature. The contents were poured in to a beaker containing crushed ice, the solid obtained was filtered washed with water and recrystallised from ethanol.

Synthesis of 2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(substitutedphenyl)acetamide (B21-B35)
3-Amino-2-(2-chlorophenyl)-quinazolin-4(3*H*)-one (0.01m) was taken in a 250ml round bottom flask refluxed with various 2-chloro-*N*-(substituted phenyl)acetamides (0.01m) in 25ml of dry pyridine for 8-12h. The reaction mixture was added into a beaker containing crushed ice, the solid obtained was filtered, washed with water and recrystallized from ethanol. All other derivatives of the series have been synthesized by similar procedure.

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-phenylacetamide (B21): Mol. formula: $C_{22}H_{17}ClN_4O_2$, Mol. Wt.: 404, Colour: pale brown, m.p.: 150-52ºC, % yield: 79.60, R_f: 0.72, λ max: 212; IR (KBr cm^{-1}) 3100 (NH str), 3010 (CH str), 1675 (cyclic C=O str), 1615 (acyclic C=O str), 1557, 1550 (NH def).

***N*-(3-Chlorophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B22):** Mol. formula: $C_{22}H_{16}Cl_2N_4O_2$, Mol. Wt.: 439, Colour: pale brown, m.p.: 154-56ºC, % yield: 68.49, R_f: 0.66, λ max: 232; IR (KBr cm^{-1}): 3090 (NH str), 3010 (CH str), 1680 (cyclic C=O str), 1612 (acyclic C=O str), 1558, 1545 (NH def).

***N*-(4-Chlorophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B23):** $C_{22}H_{16}Cl_2N_4O_2$, Mol. Wt.: 439, Colour: brown, m.p.: 147-49ºC, % yield: 45.55, R_f: 0.68, λ max: 226; IR (KBr cm^{-1}): 3112 (NH str), 3014 (CH str), 1689 (cyclic C=O str), 1614 (acyclic C=O str), 1560, 1552 (NH def); ^{1}H NMR δ ($CDCl_3$): 1.60 (s, 1H, $CH_2N\underline{H}$), 4.97 (s, 2H, $C\underline{H}_2$), 7.26-7.82 (m, 12H, Ar$\underline{H}$), 8.33 (s, 1H, CON$\underline{H}$); m/z: 439.

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(2-methylphenyl)acetamide (B24): $C_{23}H_{19}ClN_4O_2$, Mol. Wt.: 418, Colour: white, m.p.: 153-55ºC, % yield: 81.73, R_f: 0.70, λ max: 210; IR (KBr cm^{-1}): 3098 (NH str), 3011 (CH str), 1662 (cyclic C=O str), 1620 (acyclic C=O str), 1552, 1544 (NH def); ^{1}H NMR δ ($CDCl_3$): 1.58 (s, 3H, $C\underline{H}_3$), 4.97 (s, 2H, $C\underline{H}_2$), 7.26-7.82 (m, 12H, Ar$\underline{H}$), 8.37 (s, 1H, CON$\underline{H}$); m/z: 418.

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(3-methylphenyl)acetamide (B25): $C_{23}H_{19}ClN_4O_2$, Mol. Wt.: 418, Colour: white, m.p.: 148-50ºC, % yield: 43.26, R_f: 0.68, λ max: 210; IR (KBr cm^{-1}): 3099 (NH str), 3010 (CH str), 1682 (cyclic C=O str), 1614 (acyclic C=O str), 1558, 1542 (NH def); ^{1}H NMR δ ($CDCl_3$): 1.57 (s, 3H, $C\underline{H}_3$), 4.97 (s, 2H, $C\underline{H}_2$), 7.26-7.82 (m, 12H, Ar$\underline{H}$), 8.37 (s, 1H, CON$\underline{H}$), m/z: 418.

***N*-(3-Bromophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B26):** $C_{22}H_{16}BrClN_4O_2$, Mol. Wt.: 483, Colour: pale brown, m.p.: 158-60ºC, % yield: 54.16, R_f: 0.69, λ max: 214; IR (KBr cm^{-1}): 3100 (NH str), 3008 (CH str), 1680 (cyclic C=O str), 1618 (acyclic C=O str), 1554, 1543 (NH def); ^{1}H NMR δ ($CDCl_3$): 1.57 (s, 1H, $CH_2N\underline{H}$), 4.97 (s, 2H, $C\underline{H}_2$), 7.26-7.82 (m, 12H, Ar$\underline{H}$), 8.37 (s, 1H, CON$\underline{H}$); m/z: 483.

***N*-(4-Bromophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B27):** $C_{22}H_{16}BrClN_4O_2$, Mol. Wt.: 483, Colour: pale brown, m.p.: 157-59ºC, % yield: 66.66, R_f: 0.64, λ max: 213; IR (KBr cm^{-1}): 3102 (NH str), 3014 (CH str), 1673 (cyclic C=O str), 1616 (acyclic C=O str), 1551, 1542 (NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(3-nitrophenyl)acetamide (B28): $C_{22}H_{16}ClN_5O_4$, Mol. Wt.: 449, Colour: white, m.p.: 152-54ºC, % yield: 62.78, R_f: 0.63, λ max: 211; IR (KBr cm^{-1}): 3091 (NH str), 3012 (CH_2 str), 1669 (cyclic C=O str), 1612 (acyclic C=O str), 1555, 1541 (NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(4-nitrophenyl)acetamide (B29): $C_{22}H_{16}ClN_5O_4$, Mol. Wt.: 449, Colour: colourless, m.p.: 149-51ºC, % yield: 71.74, R_f: 0.75, λ max: 212; IR (KBr cm^{-1}): 3083 (NH str), 3012 (CH_2 str), 1675 (cyclic C=O str), 1613 (acyclic C=O str), 1572, 1561 (NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(4-methoxyphenyl)acetamide (B30): $C_{23}H_{19}ClN_4O_3$, Mol. Wt.: 434, Colour: dull grey, m.p.: 146-48ºC, % yield: 78.40, R_f: 0.61, λ max: 211; IR (KBr cm^{-1}): 3087 (NH str), 3011 (CH_2 str), 1672 (cyclic C=O str), 1613 (acyclic C=O str), 1559, 1546 (NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(4-methylphenyl)acetamide (B31): $C_{23}H_{19}ClN_4O_2$, Mol. Wt.: 418, Colour: brown, m.p.: 153-55ºC, % yield: 57.69, R_f: 0.63, λ max: 218; IR (KBr cm^{-1}): 3083 (NH str), 3012 (CH_2 str), 1675 (cyclic C=O str), 1612 (acyclic C=O str), 1570, 1563 (NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(2,6-dichlorophenyl)acetamide (B32): $C_{22}H_{15}Cl_3N_4O_2$, Mol. Wt.: 474, Colour: cream, m.p.: 150-52ºC, % yield: 38.29, R_f: 0.72, λ max: 216; IR (KBr cm^{-1}): 3008 (CH_2 str), 1677 (cyclic C=O str), 1612 (acyclic C=O str), 1568, 1555 (NH def).

***N*-(2-Chlorophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B33):** $C_{22}H_{16}Cl_2N_4O_2$, Mol. Wt.: 439, Colour: pale brown, m.p.: 154-56ºC, % yield: 56.16, R_f: 0.70, λ max: 218; IR (KBr cm^{-1}): 3083 (NH str), 3010 (CH str), 1675 (cyclic C=O str), 1611 (acyclic C=O str), 1571, 1560 (NH def).

***N*-(2-Bromophenyl)-2-{[2-(2-chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}acetamide (B34):** $C_{22}H_{16}BrClN_4O_2$, Mol. Wt.: 483, Colour: brown, m.p.: 148-50ºC, % yield: 75.83, R_f: 0.64, λ max: 219; IR (KBr cm^{-1}): 3079 (NH str), 3010 (CH str), 1675 (cyclic C=O str), 1603 (acyclic C=O str), 1552, 1525NH def).

2-{[2-(2-Chlorophenyl)-4-oxoquinazolin-3(4*H*)-yl]amino}-*N*-(2-nitrophenyl)acetamide (B35): $C_{22}H_{16}ClN_5O_4$, Mol. Wt.: 449, Colour: dark brown, m.p.: 131-33ºC, % yield: 49.32, R_f: 0.73, λ max: 217; IR (KBr cm^{-1}): 3083 (NH str), 3011 (CH str), 1673 (cyclic C=O str), 1612 (acyclic C=O str), 1570, 1561 (NH def).

3. Results

Antitubercular activity

The synthesized compounds B21-35 in the present study were tested for the *in vitro* anti-mycobacterial activity against *M. tuberculosis* H37Rv using the Alamar Blue assay method [17]. The compounds B21, B24 and B31 with unsubstituted phenyl, 2-methyl and 4-methyl phenyl substituents showed significant activity at a concentration of 0.2 µg/ml and it was interesting to find that all other derivatives of the series were also active at a concentration of 3.125 µg/ml. The results are shown in Table 2.

Antibacterial activity

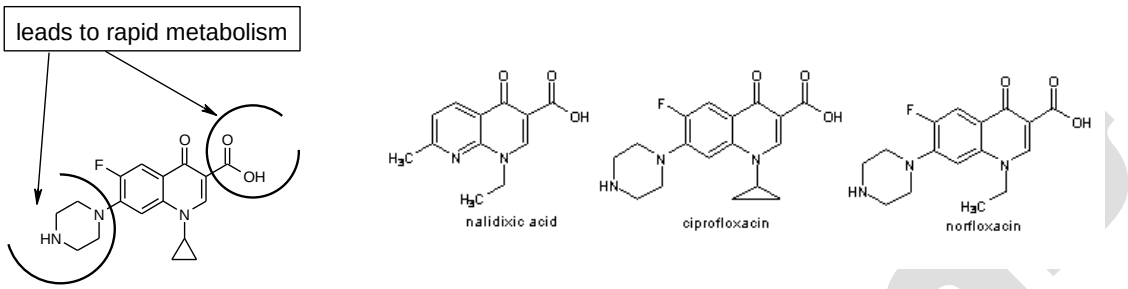
Antibacterial screening of the synthesized compounds B21-B35 was performed by the cup-plate method [18] using dimethyl sulphoxide (DMSO) as solvent. The organisms used were *Bacillus subtilis* (NCIM 2697)*, Staphylococcus aureus* (NCIM 2079)*, Escherichia coli* (NCIM 2065) and *Klebsiella pneumonia* (NCIM 5082). Ciprofloxacin was used as the standard drug for antibacterial screening study. The results are shown in Table 3.

The antibacterial activity of compounds B01-B20 is reported in our earlier research work [19, 20]. The compound B32 and B33 with 2,6-dichloro and 2-chloro phenyl substituents showed the highest degree of activity against *Bacillus subtilis* and *Staphylococcus aureus* while the compounds B30, B32 and B33 with 4-methoxy, 2,6-dichloro and 2-chloro phenyl substituents showed highest degree of activity against *Escherichia coli* and *Klebsiella pneumonia*.

4. Discussion

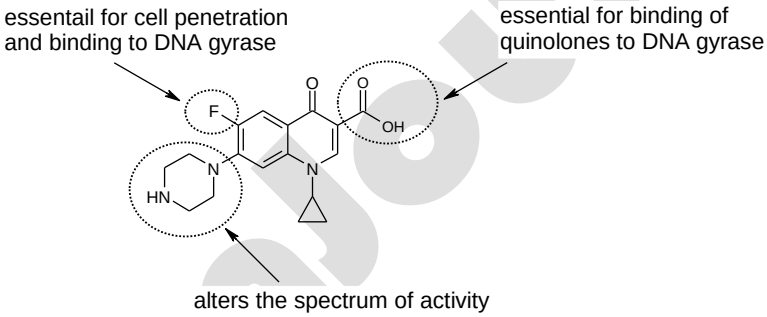
The quinolone analogs undergo metabolism by glucuronide conjugation at the 3-carboxy group producing an inactive metabolite, the piperazine ring also readily gets metabolized leading to a reduced antibacterial activity (Figure 1).

Figure 1: Quinolone antibacterials.



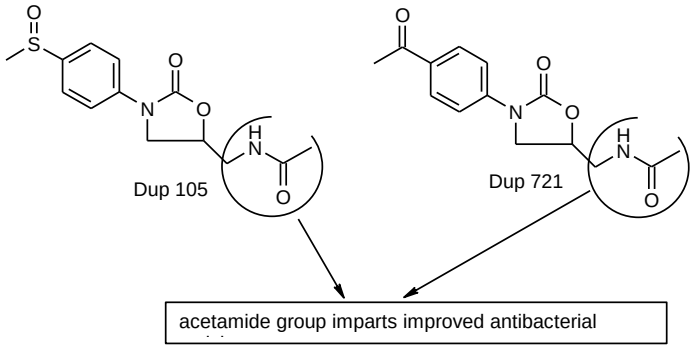
Replacement of carboxylic acid at 3rd position of quinolones with sulfonic acid, acetic acid, hydroxamic acid, sulfonamide and phosphoric acid resulted in a substantial decrease in antibacterial activity (Figure 2).

Figure 2: Effect of various groups and atom in quinolone ring.

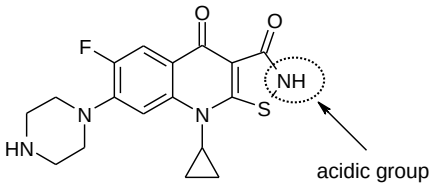


The attempt to replace the carboxylic acid with acid mimicking group like 1-*H* tetrazolyl group also resulted in a total loss of antibacterial activity. Dupont have reported DUP 105 and DUP 721 (Figure 3) with an acetamide substitution and have proved that the group imparts improved antibacterial activity.

Figure 3: Antibacterials with acetamide group.



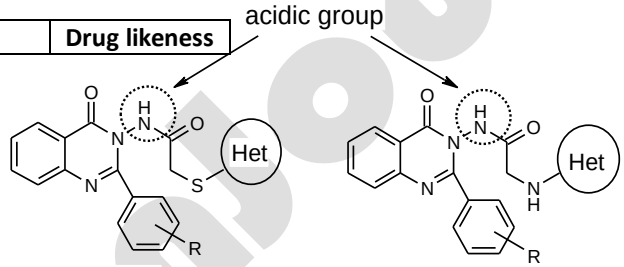
Replacement of the acid group in ciprofloxacin with bioisostere isothiazole ring (compound A-62824) has been proved to be more potent (4-10 times) than ciprofloxacin and the potency of the drug was found to be because of the acidic character of isothiazole ring [21].



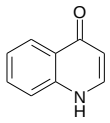
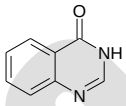
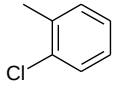
A-62824

Earlier we have reported the following prototype compounds B1-B20 containing a substituted acetamide linkage at 3rd position of quinazolinone moiety which also contributes acidic character to the molecule. Hence it was thought worthwhile to continue our research work by incorporating a substituted phenyl ring instead of carboxylic group at 3rd position of quinazolinone moiety through an acetamide linkage to enhance the potency of the molecule.

Though the ClogP value of quinolone ring is more than quinazolinone heterocyclic system, the drug likeness is less. The fluorine atom at 6th position of quinolone favours both DNA gyrase complex binding and cell penetration (lipophilicity), the ClogP value contributed by fluorine atom for the quinolone moiety is 0.06 while *o*-chlorophenyl group contributes to an extent of 2.29 which favours the lipophilicity of the molecule. So an attempt was made to retain an *o*-chlorophenyl substitution at 2nd position of quinazolinone ring.

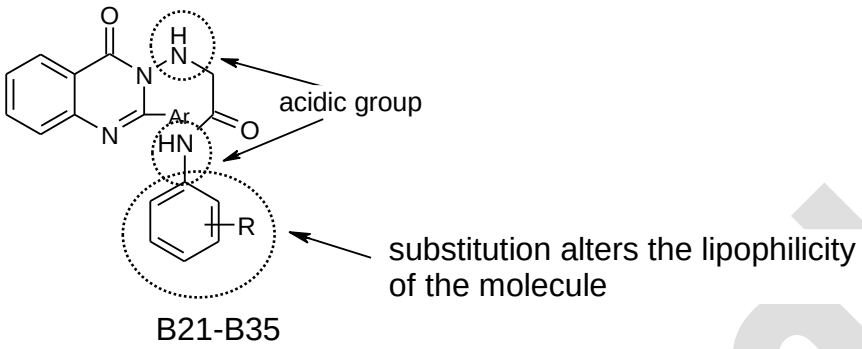


B1-B14 B15-B20

Moiety	ClogP	Drug likeness
	1.31	1.44
	0.93	2.11
F	0.06	--
	2.29	--

The potential activity of newer fluoroquinolones against drug-resistant tuberculosis led the WHO to recommend the use of levofloxacin or moxifloxacin for the treatment of extensively drug-resistant tuberculosis (XDR-TB) (defined as resistance to isoniazid, rifampicin, a fluoroquinolone and a second-line injectable drug) even

when ofloxacin resistance is present. There may be some clinical benefit from new generation agents for the treatment of *M. tuberculosis* isolates resistant to older generation fluoroquinolones [22, 23]. Hence in our continuous effort to synthesize molecules without carboxylic group at 3rd position of quinazolinone moiety, herein we report a set of compounds possessing a side chain containing two acidic protons.



B21-B35

These compounds containing amide function may undergo hydrolysis *in vivo* to release free carboxylic group that could enhance the antibacterial property. Few of the synthetic antibacterials like nitrofurantoin lead to interstitial pulmonary fibrosis in patients on chronic medication [24, 25] which is due to the generation of oxygen radicals as a result of redox cycling of the drug in the lungs. So, to acquire a better knowledge on the novel compounds, the antioxidant activity of the synthesized molecules was evaluated. The Table 1 shows the ClogP value, drug likeness and drug score of the compounds that have been reported earlier and the newly synthesized compounds.

Our preliminary data indicate that the compounds B01-20 possessing a heterocyclic ring system in the side chain attached through acetamide or thioacetamide linkage to the quinazolinone moiety were active against *M. tuberculosis* at a higher concentration (25µg/ml) whereas the compounds B21-35 containing a simple aromatic system with acidic proton in the side chain showed promising activity at a minimum concentration of 0.2-3.125 µg/ml. It was interesting to observe that the replacement of the heterocyclic ring with substituted aryl group has shown promising antitubercular activity against *M. tuberculosis*. Hence, these compounds can be considered as pharmacophore unit and exploited further to obtain novel antitubercular agent.

Competing Interests
None declared.

Authors' Contributions
Both authors contributed equally to this work.

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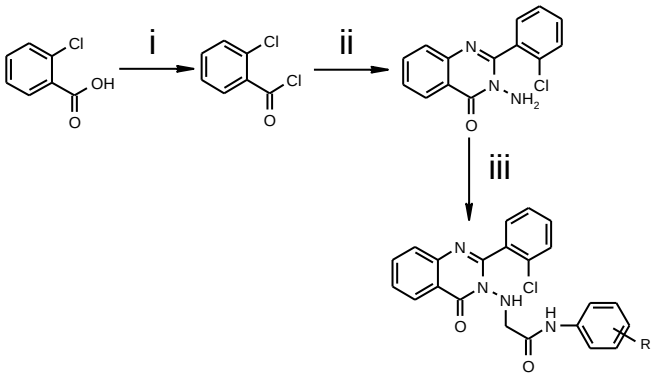
Figure 4: Scheme for synthesis of compounds B21-B35**.**

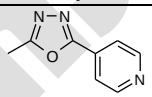
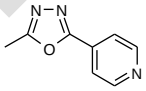
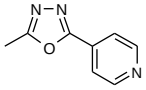
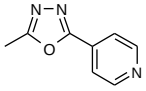
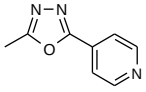
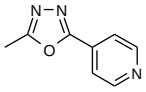
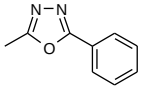


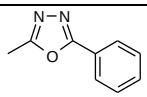
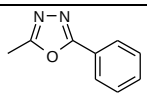
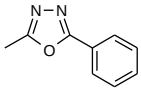
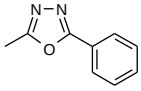
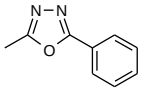
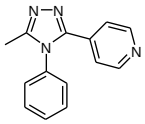
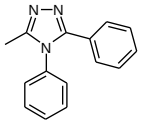
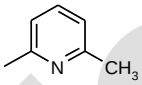
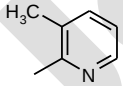
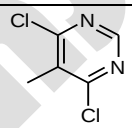
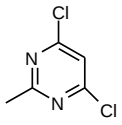
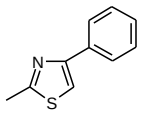
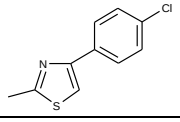
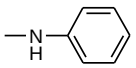
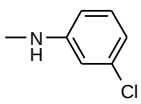
B21-35

Comp.Code	R	Comp.Code	R
B21	H	B31	4-CH_3
B22	3-Cl	B32	2,6-Cl_2
B23	4-Cl	B33	2-Cl
B24	2-CH_3	B34	2-Br
B25	3-CH_3	B35	2-NO_2
B26	3-Br		
B27	4-Br		
B28	3-NO_2		
B29	4-NO_2		
B30	4-OMe		

(i):thionyl chloride, benzene, (ii):anthranilic acid, dry pyridine, hydrazine hydrate,
(iii):various substituted chloroacetamides

Table 1: Evaluation of ClogP, drug likeness and drug score of compounds B1-B35.

Compound	R	Het/Ar	ClogP	Drug likeness	Drug score
B1	H		2.06	4.75	0.43
B2	2-Cl		2.67	4.42	0.35
B3	4-Cl		2.67	4.77	0.35
B4	2-CH_3		2.37	3.82	0.39
B5	4-CH_3		2.37	2.58	0.38
B6	3-NO_2		--	--	--
B7	H		3.14	4.86	0.36

B8	2-Cl		3.75	4.55	0.30
B9	4-Cl		3.75	4.90	0.30
B10	2-CH_3		3.45	3.96	0.33
B11	4-CH_3		3.45	2.71	0.32
B12	3-NO_2		--	--	--
B13	H		3.03	4.78	0.27
B14	H		4.1	4.88	0.18
B15	H		1.85	5.02	0.59
B16	H		1.75	5.49	0.59
B17	H		1.72	3.72	0.33
B18	H		2.24	5.11	0.32
B19	H		3.30	5.73	0.32
B20	H		3.91	6.52	0.26
B21	2-Cl		2.64	3.54	0.502
B22	2-Cl		3.26	5.12	0.413

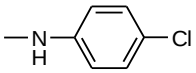
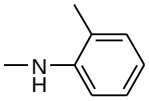
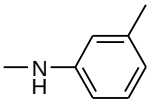
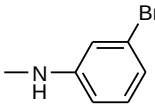
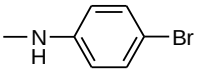
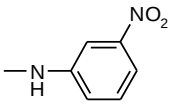
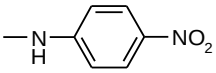
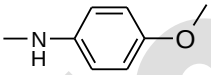
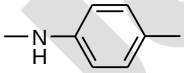
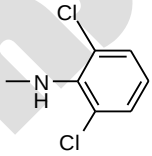
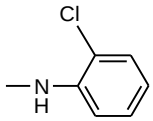
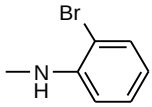
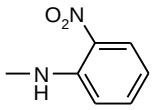
B23	2-Cl		3.26	5.91	0.414
B24	2-Cl		2.96	4.96	0.463
B25	2-Cl		2.96	4.8	0.463
B26	2-Cl		3.34	1.8	0.349
B27	2-Cl		3.34	3.22	0.368
B28	2-Cl		--	--	--
B29	2-Cl		--	--	--
B30	2-Cl		2.54	3.92	0.232
B31	2-Cl		2.96	3.78	0.275
B32	2-Cl		3.87	5.88	0.331
B33	2-Cl		3.26	4.83	0.33
B34	2-Cl		3.34	1.34	0.336
B35	2-Cl		--	--	--

Table 2: Antitubercular activity of the compounds B21-35.

Compounds	100	50	25	12.5	6.25	3.125	1.6	0.8	0.4	0.2
B21	S	S	S	S	S	S	S	S	S	S
B22	S	S	S	S	S	S	S	S	R	R
B23	S	S	S	S	S	S	S	S	R	R
B24	S	S	S	S	S	S	S	S	S	S
B25	S	S	S	S	S	S	R	R	R	R
B26	S	S	S	S	S	S	R	R	R	R
B27	S	S	S	S	S	S	S	S	R	R
B28	S	S	S	S	S	S	S	S	R	R
B29	S	S	S	S	S	S	S	S	R	R
B30	S	S	S	S	S	S	S	S	S	R
B31	S	S	S	S	S	S	S	S	S	S
B32	S	S	S	S	S	S	S	S	R	R
B33	S	S	S	S	S	S	S	S	R	R
B34	S	S	S	S	S	S	S	S	R	R
B35	S	S	S	S	S	S	S	R	R	R
INH	S	S	S	S	S	S	S	S	S	S

Table 3: Antibacterial activity of the compounds B21-35.

Compound Code	Zone of Inhibition in mm			
	Bacillus subtilis **(NCIM 2697)**	***Staphylococcus aureus*** **(NCIM 2079)**	***Escherichia coli*** **(NCIM 2065)**	***Klebsiella pneumonia*** **(NCIM 5082)**
B21	14	14	--	14
B22	--	14	--	10
B23	--	14	--	14
B24	12	12	12	14
B25	12	12	12	12
B26	12	14	12	14
B27	12	14	12	12
B28	12	12	12	14
B29	14	16	12	14
B30	12	16	12	16
B31	12	12	14	14
B32	16	16	12	16
B33	16	14	18	14
B34	12	12	14	14
B35	14	14	14	12
Ciprofloxacin	27	29	31	31