CHAPTER–III

PART–I

Synthesis of Pyrazolyl-1,3,4-oxadiazole Carboxamide Analogues
3.1.1 Introduction

Identification of novel structure leads that may be of use in designing new, potent and broad spectrum antimicrobial agents remains a major challenge for medicinal chemistry researchers. In this view, the discovery of the natural 4-hydroxypyrazole C-glycoside antibiotic pyrazofurin (Figure 3.1); has provided a basis for more rationale design and synthesis of new pyrazoles as potential antimicrobial.

![Figure 3.1: Structure of pyrazofurin.](image)

Survey of the literature revealed that linked biheterocyclic compounds containing pyrazole to possess biological activity are often reported. Recently pyrazole incorporated thiazole,\(^1\) thia diazole,\(^2\) 1,2,4-oxadiazole,\(^3\) 1,2,4-triazoles and benzo xazoles\(^4\) were synthesized and observed in the enhancement of pharmacological effect.

Amide bonds are neutral, stable and have both hydrogen-bond accepting and donating properties. Hence, they play a crucial role in the composition of biological systems and are present in more than 25\% of the known drugs\(^5\) including major marketed drug Atorvastatin which blocks the production of cholesterol.\(^6\)
In our laboratory Rai et al., synthesized the derivatives of pyrazole-4-carboxylate by cycloaddition reaction of various benzaldehyde hydrazone with ethyl acetoacetate using chloramine-T (CAT) as oxidant. They have also synthesized 2-amino-5-substituted-1,3,4-oxadiazoles using various benzaldehyde semicarbazone using CAT.

Encouraged by these observations and in continuation of our research work on the synthesis of heterocyclic compounds containing multi-structure for biological activity, we thought of synthesizing a new class of heterocycles, wherein potent 1,3,4-oxadiazole moiety is linked to pyrazole moiety at C-4 position with an amide bond to see the additive effect of these rings towards the antimicrobial activity, which is the current passion being accomplished in most of the drug discoveries.

### 3.1.2 Plan of the Synthesis

5-phenyl-1,3,4-oxadiazol-2-amines 70(a-c) were synthesized by heating a mixture benzaldehyde I(a-c) and semicarbazide in presence of chloramine-T over a period of 3 to 4h as shown in **Scheme 4.1**.

**Scheme 4.1.** Synthesis of 5-phenyl-1,3,4-oxadiazol-2-amines 70(a-c)
Here we describe the synthesis of a series of novel 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide derivatives.

![Scheme 4.2. Synthesis of 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide](image)

3.1.3 Discussion on the synthesis of 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

1,3,4-oxadiazoles are very important class of heterocyclic compounds. Due to their interesting biological activities several methods for the preparation of substituted 2-amino-5-phenyl-1,3,4-oxadiazole have been described. Among several reported methods, the one with oxidative ring closure reaction of various aryl semicarbazone with CAT (K.M.L. Rai, et al.) is best suited. By utilizing this method we have synthesized oxadiazoles 70(a-c).
The synthesis of title compounds is as outlined in Scheme 4.2. The title compounds were synthesized by condensation of equal mole of 5-methyl-1,3-diphenyl-1H-pyrazole-4-carbonyl chloride (73a) and 2-amino-5-phenyl-1,3,4-oxadiazoles (70a) in presence of triethylamine (one equivalent) as a base and dry DMF (10mL) as solvent. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was distilled to remove the excess of solvent, the crude solid thus obtained was recrystallised from suitable solvent to get pure solid. The newly synthesized compounds are in spectral agreement with the reported ones. Soon after the synthesis of oxadiazoles they were condensed with pyrazole-4-carbonyl chloride 73(a-c) using triethylamine.

The IR spectra of 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide derivatives illustrate -CO and -NH amide stretching bands at 1600-1630 cm\(^{-1}\) and 3400-3490 cm\(^{-1}\) respectively. In \(^1\)H NMR spectra, all protons were seen according to the expected chemical shift and integral values. Compound 72(a-c) showed the absence of methyl and methylene protons of ethyl group at \(\delta\) 1.29-1.35 and 4.10-4.32 ppm respectively. Beside they showed the presence of singlet -OH peak at \(\delta\) 11.02-11.05 ppm. Similarly compounds 73(a-c) and 74(a-e) showed the absence of singlet -OH peak at \(\delta\) 11.02-11.05 ppm. This confirms the structure of 72(a-c), 73(a-c) and 74(a-e). In addition to this, structure of 74(a-e) was confirmed by the appearance of amide -NH peak at \(\delta\) 10.02-10.12 ppm.
3.1.4 Experimental results for the synthesis of 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

General

All chemicals were obtained from commercial suppliers and used without further purification. Melting points were determined in open capillaries on a Buchi oil melting point apparatus and are uncorrected. Reactions were monitored by using TLC on aluminum sheets precoated with silica gel 60 F254 (0.2 mm, Merck). Chromatographic spots were visualized by UV light and/or with iodine. For column chromatography, silica gel of 100-200 mesh size was used. 1H NMR spectra were acquired on a Bruker Avance 400 MHz instrument in DMSO-d6 or CDCl3. 13C NMR spectra were recorded on a Bruker AMX-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent as the internal reference. Mass spectrometry was performed with a Bruker-Franzen Esquire LC mass spectrometer unless otherwise stated.

General procedure for the synthesis of 5-phenyl-1,3,4-oxadiazol-2-amine (70a):

To a mixture of the benzaldehyde (Ia, 0.12g, 1.00mmol) and semicarbazide (1.00mmol) was added CAT (1.00mmol) in portions over 0.5h at
80-90°C and the mixture was stirred at this temperature for 3 to 4h. Then the reaction mixture was cooled, water/ice was added and it was the solid thus obtained was finally recrystallized in ethyl alcohol to give pure 5-phenyl-1,3,4-oxadiazol-2-amine 70a as a white solid in 70% (0.12g) yield, mp 237-239°C lit mp 238-240°C.\(^8\)

**5-(4-chlorophenyl)-1,3,4-oxadiazol-2-amine (70b):**

Obtained from heating 4-chlorobenzaldehyde (Ib, 0.14g, 1.00mmol) and semicarbazide, (1.00mmol) in presence of CAT at 80-90°C for about 3 to 4h as white solid in 88% yield (0.18g), mp 229-231°C lit mp 231-234°C.\(^10\)

**5-(p-tolyl)-1,3,4-oxadiazol-2-amine (70c):**

Obtained from heating 4-methylbenzaldehyde (Ie, 0.12g, 1.00mmol) and semicarbazide (1.00mmol) in presence of CAT at 80-90°C for about 3 to 4h as brown solid in 72% (0.13g) yield, mp 208-212°C lit mp 210-218°C.\(^10\)
General procedure for synthesis of 5-methyl-1,3-diphenyl-1H-pyrazole-4-carboxylic acid (72a):

Ethyl 5-methyl-1,3-diphenyl-1H-pyrazole-4-carboxylate (71a, 1.00g, 3.26mmol) and 10% NaOH (10mL) in presence of alcohol (20mL) were stirred at room temperature for about 4hr. After the completion of the reaction (monitored by TLC), the solution was neutralized with HCl to give off white solid pyrazole-4-carboxylic acid (72a). The pyrazole (72a) was white solid in 92% yield (0.83g) showed mp 198-200°C, in IR (Nujol): 2870-3200 cm\(^{-1}\) (\(-\text{OH}\) acid), 1698-1710 cm\(^{-1}\) (C=O, acid), 1620 cm\(^{-1}\) (C=N), 1608 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (J, Hz): 2.71 (s, 3H), 7.05-7.26 (m, 5H), 7.65-7.78 (m, 5H), 11.02 (s, 1H); MS (relative intensity %): m/z for C\(_{17}\)H\(_{14}\)N\(_2\)O\(_2\): 279.3 [M+H]\(^+\) (100). Anal. % Calc: C, 73.37; H, 5.07; N, 10.07; Found: C, 73.35, H, 5.06, N, 10.10%.

3-(4-chlorophenyl)-5-methyl-1-phenyl-1H-pyrazole-4-carboxylic acid (72b):

Obtained from ethyl 3-(4-chlorophenyl)-5-methyl-1-phenyl-1H-pyrazole-4-carboxylate (71b, 1.00g, 2.93mmol) and 10% NaOH as white solid in 93% yield (0.85g), mp 172-174°C, in IR (Nujol): 2870-3200 cm\(^{-1}\) (\(-\text{OH}\) acid), 1695-1705 cm\(^{-1}\) (C=O, acid), 1615 cm\(^{-1}\) (C=N); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (J, Hz): 2.70 (s, 3H), 6.98-7.00 (d, 2H, \(J = 8.0\)), 7.18-7.20 (d, 2H, \(J = 8.0\)), 7.44-7.60 (m, 5H),
11.05 (s, 1H); MS (relative intensity %): m/z for C\textsubscript{17}H\textsubscript{13}ClN\textsubscript{2}O\textsubscript{2}; 312.1 [M+] (100), 314.1 [M+2]. Anal. % Calc: C, 66.86; H, 5.13; N, 8.18; Found: C, 66.70; H, 5.01; N, 8.01.

\textbf{5-methyl-1-phenyl-3-(p-tolyl)-1H-pyrazole-4-carboxylic acid (72c):}

Obtained from ethyl 5-methyl-1-phenyl-3-p-tolyl-1H-pyrazole-4-carboxylate (71c, 1.00g, 3.12mmol) and 10% NaOH as light brown solid in 90% yield (0.82g), mp 140-142°C, in IR (Nujol): 2870-3200 cm\textsuperscript{-1} (-OH acid), 1698-1710 cm\textsuperscript{-1} (C=O, acid), 1620 cm\textsuperscript{-1} (C=N), 1610 cm\textsuperscript{-1} (C=C); \textsuperscript{1}H NMR (CDCl\textsubscript{3}), \delta ppm (J, Hz): 2.16 (s, 3H), 2.72 (s, 3H), 7.06-7.08 (d, 2H, J = 8.0), 7.28-7.30 (d, 2H, J = 8.0), 7.42-7.64 (m, 5H), 11.05 (s, 1H, OH); MS (relative intensity %): m/z for C\textsubscript{18}H\textsubscript{16}N\textsubscript{2}O\textsubscript{2}; 293.1 [M+H]\textsuperscript{+}(100); Anal. % Calc: C, 73.85; H, 5.50; N, 9.38; Found: C, 73.65; H, 5.62; N, 9.58.

\textbf{General procedure for synthesis of 5-methyl-1, 3-diphenyl-1H-pyrazole-4-carbonyl chloride (73a):}

5-methyl-1,3-diphenyl-1H-pyrazole-4-carboxylic acid (72a, 1.00g, 3.59mmol) was refluxed with SOCl\textsubscript{2} (0.50 mL) using CH\textsubscript{2}Cl\textsubscript{2} (10mL) as a solvent for about 4-5 hr.

After the reaction was completed (monitored by TLC), the reaction mixture was distilled under reduced pressure to remove excess solvent and SOCl\textsubscript{2}. The crude product obtained was recrystalised from hot ethanol to get 73a as white solid.
in 85% yield (0.90g), mp 86-88°C. IR (Nujol): 1690-1700 cm\(^{-1}\) (C=O, acid chloride), 1620 cm\(^{-1}\) (C=N), 1608 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (\(J, \text{ Hz}\)): 2.70 (s, 3H), 7.05-7.26 (m, 5H), 7.65-7.78 (m, 5H); MS (relative intensity %): m/z for C\(_{17}\)H\(_{13}\)ClN\(_2\)O: 296.7 [M+] (100), 298.7 [M+2]; Anal. % Calc: C, 68.81; H, 4.42; N, 9.44; Found: C, 68.79; H, 4.40; N, 9.48.

3-(4-chlorophenyl)-5-methyl-1-phenyl-1H-pyrazole-4-carbonyl chloride (73b):

Obtained from 3-(4-chlorophenyl)-5-methyl-1-phenyl-1H-pyrazole-4-carboxylic acid (72b, 1.00g, 3.19mmol) as yellow solid in 83% yield (0.88g), mp 110-112°C. IR (Nujol): 1695-1710 cm\(^{-1}\) (C=O, acid chloride), 1620 cm\(^{-1}\) (C=N), 1610 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (\(J, \text{ Hz}\)): 2.70 (s, 3H), 6.98-7.00 (d, 2H, \(J = 8.0\)), 7.08-7.10 (d, 2H, \(J = 8.0\)), 7.40-7.60 (m, 5H); MS (relative intensity %): m/z for C\(_{17}\)H\(_{12}\)Cl\(_2\)N\(_2\)O: 330.2 [M+] (100), 332.2 [M+2], 334.2 [M+4]; Anal. % Calc: C, 61.65; H, 3.65; N, 8.46; Found: C, 61.62; H, 3.66; N, 8.48.
5-methyl-1-phenyl-3-(p-tolyl)-1H-pyrazole-4-carbonyl chloride (73c):

Obtained from 5-methyl-1-phenyl-3-(p-tolyl)-1H-pyrazole-4-carboxylic acid (72c, 1.00g, 3.42mmol) as buff color solid in 78% yield (0.83g), mp 78-80°C; IR (Nujol): 1700-1710 cm⁻¹ (C=O, acid), 1620 cm⁻¹ (C=N), 1610 cm⁻¹ (C=C); ¹H NMR (CDCl₃), δ ppm (J, Hz): 2.10 (s, 3H), 2.60 (s, 3H), 7.06-7.08 (d, 2H, J = 8.0 ), 7.28-7.30 (d, 2H, J = 8.0), 7.40-7.65 (m, 5H); MS (relative intensity %): m/z for C₁₈H₁₅ClN₂O: 310.1 [M+] (100), 312.1 [M+2]; Anal. % Calc: C, 69.57; H, 4.86; N, 9.01; Found: C, 69.54; H, 4.88; N, 9.02.

General procedure for synthesis of 5-methyl-1,3-diphenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide (74a)

The synthesis of title compound is as outlined in Scheme 4.2. The compound (74a) was synthesized by the condensation of 5-methyl-1,3-diphenyl-1H-pyrazole-4-carbonyl chloride (73a, 1.00g, 3.35 mmol) and 2-amino-5-phenyl-1,3,4-Oxadiazoles (70a, 0.54g, 3.35mmol) in presence of triethylamine (one equivalent) as a base and dry DMF (10mL) as solvent. After stirring at room temperature for 5-6 hr, (monitored by TLC) the reaction mixture was added to ice cold water. Then the reaction mixture was extracted with
ether (3 x 30mL), washed with water and the organic layer was passed through anhydrous sodium sulphate. Finally a compound 74a was achieved, as white crystalline solid in 75% yield (1.06g) after drying the organic layer, mp 174-176°C. IR (Nujol): 1680-1690 cm\(^{-1}\) (C=O amide), 3310 cm\(^{-1}\) (NH amide), 1620 cm\(^{-1}\) (C=N), 1605 cm\(^{-1}\) (C=C); \(^1\)H NMR (DMSO-\(d_6\)), \(\delta\) ppm (J, Hz); 2.81 (s, 3H), 7.12-7.45 (s, 5H), 7.46-7.68 (m, 5H), 7.60-7.91 (m, 5H), 10.12 (s, 1H) (Figure 3.2); MS (relative intensity %): m/z for C\(_{25}\)H\(_{19}\)N\(_5\)O\(_2\): 422.1 [M+H]\(^+\) (100) (Figure 3.3); Anal. % Calc: C, 71.25; H, 4.54; N, 16.62; Found: C, 71.26; H, 4.52; N, 16.63.

The same procedure was used in all cases.

**3-(4-chlorophenyl)-5-methyl-1-phenyl-N-(5-phenyl-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide (74b)**

Obtained by the condensation of 3-(4-chlorophenyl)-5-methyl-1-phenyl-1H-pyrazole-4-carbonyl chloride (73b, 1.00g, 3.01mmol) with 2-amino-5-phenyl-1,3,4-oxadiazoles (70a, 0.48g, 3.01mmol) as a off white solid in 78% yield (1.07g), mp 186-188°C. IR (Nujol): 1680-1690 cm\(^{-1}\) (C=O amide), 3320-3325 cm\(^{-1}\) (NH amide), 1620 cm\(^{-1}\) (C=N), 1610 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (J, Hz); 2.80 (s, 3H), 6.98-7.00 (d, 2H, J = 8.0), 7.08-7.10 (d, 2H, J = 8.0), 7.46-7.68 (m, 5H), 7.80-7.91 (m, 5H), 10.02 (s, 1H) (Figure 3.4); MS
(relative intensity %): m/z for C_{25}H_{18}ClN_{5}O_{2}: 455.1 [M+] (100), 457.1 [M+2] (Figure 3.5); Anal. % Calc: C, 65.86; H, 3.98; N, 15.36; Found: C, 65.85; H, 3.92; N, 15.43.

5-methyl-1-phenyl-N{(5-phenyl-1,3,4-oxadiazol-2-yl)-3-(p-tolyl)-1H-pyrazole-4-carboxamide (74c)}

Obtained by the condensation of 5-methyl-1-phenyl-3-(p-tolyl)-1H-pyrazole-4-carbonyl chloride (73c, 1.00g, 3.22mmol) with 2-amino-5-phenyl-1,3,4-oxadiazoles (70a, 0.52g, 3.22mmol) as a buff colored solid in 80% yield (1.12g).

mp 204-206°C; IR (Nujol): 1675-1690 cm\(^{-1}\) (C=O amide), 3310-3325 cm\(^{-1}\) (NH amide), 1620 cm\(^{-1}\) (C=N), 1610 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (J, Hz): 2.60 (s, 3H), 2.79 (s, 3H), 7.06-7.08 (d, 2H, \(J = 8.0\)), 7.28-7.30 (d, 2H, \(J = 8.0\)), 7.30-7.55 (m, 5H), 7.60-7.91 (m, 5H), 10.02 (s, 1H); MS (relative intensity %): m/z for C_{26}H_{21}N_{5}O_{2}: 436.4 [M+H]^+(100) Anal. % Calc: C, 71.71; H, 4.86; N, 16.08; Found: C, 71.63; H, 4.90; N, 16.12.
$N\{5\{4\text{-chlorophenyl}\}\{1,3,4\text{-oxadiazol-2-yl}\}\{5\text{-methyl-1,3-diphenyl-}1H\text{-pyrazole-4-carboxamide (74d)}$

Obtained by the condensation of 5-methyl-1,3-diphenyl-1$H$-pyrazole-4-carbonyl chloride (73a, 1.00g, 3.37mmol) with 5-(4-chlorophenyl)-1,3,4-oxadiazol-2-amine (70b, 0.64g, 3.37mmol) as a off white solid in 82% yield (1.26g), mp 194-196°C; IR (Nujol): 1670-1685 cm$^{-1}$ (C=O amide), 3305-3325 cm$^{-1}$ (NH amide), 1620 cm$^{-1}$ (C=N), 1605 cm$^{-1}$ (C=C); $^1H$ NMR (CDCl$\text{3}$), $\delta$ ppm (J, Hz); 2.81 (s, 3H), 6.88-6.90 (d, 2H, $J = 8.0$), 7.10-7.12 (d, 2H, $J = 8.0$), 7.40-7.60 (m, 5H), 7.72-7.91 (m, 5H), 10.11 (s, 1H); MS (relative intensity %): m/z for C$_{25}$H$_{18}$ClN$_{5}$O$_{2}$: 455.4 [M+] (100), 457.2 [M+2]; Anal. % Calc: C, 65.86; H, 3.98; N, 15.36; Found: C, 65.80; H, 3.99; N, 15.41.

$5\text{-methyl-1,3-diphenyl-N\{5\{p\text{-tolyl}\}\{1,3,4\text{-oxadiazol-2-yl}\}\1H\text{-pyrazole-4-carboxamide (74e)}$

Obtained by the condensation of 5-methyl-1,3-diphenyl-1$H$-pyrazole-4-carbonyl chloride (73a, 1.00g, 3.37mmol) with 5-(p-tolyl)-1,3,4-oxadiazol-2-amine (70c, 0.59g, 3.37mmol) as a light brown color solid in 79% yield (1.16g), mp 178-
180°C; IR (Nujol): 1675-1685 cm\(^{-1}\) (C=O amide), 3310-3325 cm\(^{-1}\) (NH amide), 1620 cm\(^{-1}\) (C=N), 1605 cm\(^{-1}\) (C=C); \(^1\)H NMR (CDCl\(_3\)), \(\delta\) ppm (J, Hz): 2.70 (s, 3H), 2.61 (s, 3H), 6.98-7.00 (d, 2H, \(J = 8.0\)), 7.20-7.22 (d, 2H, \(J = 8.0\)), 7.42-7.65 (m, 5H), 7.70-7.81 (m, 5H), 10.10 (s, 1H); MS (relative intensity %): m/z for C\(_{26}\)H\(_{21}\)N\(_5\)O\(_2\): 436.2 [M+H]\(^+\) (100); Anal. % Calc: C, 71.71; H, 4.86; N, 16.08. Found: C, 71.68; H, 4.88; N, 16.09.
Figure 3.2: $^1$H NMR spectrum of compound 74a
Figure 3.3: Mass spectrum of compound 74a
Figure 3.4: $^1$H NMR spectrum of compound 74b
Figure 3.5: Mass spectrum of compound 74b
CHAPTER–III

PART–II

Biological Activity of Pyrazolyl-1,3,4-oxadiazole Carboxamide Analogues
3.2.1 Antimicrobial activity

3.2.1.1 Evaluation of antimicrobial activity of compounds 74(a-e)

Materials and methods:

Antibacterial activity was determined by cup diffusion method on nutrient agar medium. The sterile medium (20mL) was poured into a 9 cm petriplates. The medium was allowed to cool in a sterile condition and plates were then inoculated with 1x10^5 cfu cultures of test bacteria. The concentration of bacterial cells in the suspension was adjusted to minimum of 1x10^5 cfu/mL in nutrient broth solution. Agar cup of 5 mm diameter were made in the plates. Each test sample was dissolved in DMF, 50 µl of test solution containing 15 mg of the test compound were placed in each cup. The plates were left to stay for an hour in order to facilitate the diffusion of the drug solution. Negative controls were prepared using DMF then the plates were incubated at 37°C for 24 hr. The zone of inhibition if any against the test bacteria were measured in mm. Bacitracin and Amoxycillin were used as positive reference to determine the sensitivity of each bacterial species tested.

The synthesized compounds 74(a-e) were passed through a general antibacterial screen. Twelve human pathogenic bacteria were chosen to evaluate the synthesized aryl pyrazole-oxadiazole analogues for antibacterial activity. All compounds were tested at a concentration of 15mg. Bacitracin and Amoxycillin, the standard drugs, were also screened against the bacteria and the results, which are qualitative in nature, are as shown in Table 3.1. The control
Bacitracin exhibited activity towards *Pseudomonas aeruginosa*, *S. paratyphi B* and *Streptococcus faecalis* bacterial strains only.

In all the determinations tests were performed in six replicate and the results were taken as a mean of at least three determinations.

### 3.2.1.2 Discussion on antimicrobial activity of compounds 74(a-e)

The antimicrobial activity results are summarized in Table 3.1. The results revealed that, compounds 74c and 74e with methyl group at para position in phenyl ring has exhibited highest activity against *Shigella boydii* and little less against *Staphylococcus aureus*, *S. paratyphi A* and *Proteus mirabilis*. On the other hand compounds 74b and 74d with chloro group at para position in phenyl ring have exhibited activity against *Shigella boydii*, *Salmonella typhi*. 
<table>
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<th>Sl. No</th>
<th>Compd.</th>
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<th>74b</th>
<th>74c</th>
<th>74d</th>
<th>74e</th>
<th>Bacitracin</th>
<th>Amoxycillin</th>
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<td><em>Salmonella typhi</em></td>
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<td>18.62±0.18</td>
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<td>37.55±0.05</td>
<td>15.70±0.22</td>
<td>29.66±0.11</td>
<td>0.00±0.00</td>
<td>18.13±0.48</td>
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<td>08</td>
<td><em>Proteus mirabilis</em></td>
<td>11.50±0.35</td>
<td>19.56±0.11</td>
<td>35.65±0.08</td>
<td>10.33±0.16</td>
<td>35.50±0.36</td>
<td>0.00±0.00</td>
<td>20.25±0.16</td>
</tr>
<tr>
<td>09</td>
<td><em>Streptococcus faecalis</em></td>
<td>12.16±0.22</td>
<td>23.33±0.18</td>
<td>17.56±0.15</td>
<td>12.37±0.14</td>
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<td>11.50±0.18</td>
<td>18.75±0.31</td>
</tr>
<tr>
<td>10</td>
<td><em>S. paratyphi</em> A</td>
<td>15.66±0.15</td>
<td>28.56±0.25</td>
<td>37.55±0.07</td>
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<td>29.66±0.11</td>
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<tr>
<td>11</td>
<td><em>Shigella boydii</em></td>
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<td>35.50±0.27</td>
<td>38.50±0.12</td>
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<tr>
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<td>22.25±0.16</td>
</tr>
</tbody>
</table>

Zone of inhibition (Mean six replicate ± standard error). \( p<0.05 \)
3.3.1 References


