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Synthesis of Dihydropyrimidinine derivatives and 5-substituted-1,3,4-oxadiazole clumped pyrazole as potential bioactive agents

Mr.Sk.Johnmiya[1], Mrs Gowthami[2], Mr.B.Ramaji Rao[3], Mrs.K.Kamala Kumari[4]

ASSIT.PROFESSOR[1,2,3,4]
H&S(Chemistry)
SWARNA BHARATHI INSTITUTE OF SCIENCE & TECHNOLOGY (SBIT)

Abstract: 4-Fluorophenylpyrazole clubbed 1,3,4-oxadiazole and 3,4-dihydropyrimidin-2(1H)-ones were generated by cyclizing Biginelli-type adducts. Structure assignments were made using the standard spectrum methods. Using microplate alamar blue assay and broth microdilution bioassay, respectively, the scaffolds were examined in vitro for their antibacterial and antitubercular activities. The -OH and -CH3 groups of compounds 3j and 3l showed considerable cytotoxicity on VERO cells, which raises questions about their antibacterial and antitubercular capabilities.

INTRODUCTION

A number of infectious illnesses have significant therapeutic challenges due to microbial resistance. One of the greatest dangers to human life, according to the World Health Organisation (WHO), is antimicrobial drug resistance (AMR). In the realm of drug development programmes, structural alterations to current medications have shown remarkable outcomes. Accordingly, the most effective method for creating new, more powerful drugs is to use a molecular hybridization strategy to create scaffold architecture that is completely unique.1, 2 The synthesis of dihydropyrimidines (DHPMs) with diverse bioactivities has recently attracted the interest of many medicinal chemists, and the Biginelli type reaction in particular.3-5 The varied pharmacological properties of pyrazoles, which include antibacterial, antidepressant, anticonvulsant, antipyretic, anti-influenza, and anticancer actions, have made them a prominent motif in medicinal chemistry and a hub for synthetic heterocycles.6-8 Several catalysts, including Sc(OTf)3, Mg(ClO4)2, and H2SO4, were used in a multicomponent process to produce pyrazole derivatives.9-11

Because of its metabolic profile and capacity to form hydrogen bonds with the receptor site, oxadiazole has been a widely used pharmacophore in recent years. Numerous biological actions, including hypoglycaemic, anti-HIV, analgesic, anti-inflammatory, and antitubercular effects, are generated by the presence of an azole group in oxadiazole, which increases its lipophilicity and impacts its easy ability to target.12,13 Oxadiazole have shown great promise as inhibitors of key biological targets, such as tyrosinase, MAO, and cathepsin K.14–19.

Keywords: 1,3,4-Oxadiazole, 3,4-dihydropyrimidin-2(1H)-one, pyrazole, antimicrobial, antitubercular, minimum inhibitory concentration (MIC).

EXPERIMENTAL

No further purification was performed on the compounds that were acquired from Aldrich and E. Merck. Distillation was carried out using Buchi Rotavapor. The Gallenkamp apparatus was used to determine the melting points, and these values have not been revised. The reaction was seen under ultraviolet light (λ 254 and 365 nm) or iodine vapour to ensure that all compounds were pure and that the reaction had finished on aluminum-coated TLC plates G60, F245 (E. Merck) with an eluent ratio of 7:3. The Perkin-Elmer 2400 CHN analyzer was used for the elemental analysis. The chemical

shifts were measured using TMS as a reference standard, and 1H NMR spectra were captured using a Bruker Avance II 400 MHz. The 13C NMR spectra were recorded on a Varian Mercury-400, 100 MHz, using DMSO-d6 as the solvent. A Shimadzu LCMS 2010 spectrometer was used for mass spectra scanning, while a Perkin-Elmer FT-IR spectrophotometer was used for infrared spectra recording. conc. H_2SO_4 and allowed to stir for 5 h at 100 °C. After cooling, the reaction mixture was poured into ice-cold water. Product, obtained as off-white precipitate, was filtered, washed with water, dried and recrystallized from ethanol (95 %) to obtain compound **2**.

Yield: 73 %, m.p. 224-225 ºC. IR (KBr): 3454, 3340 (N-
H), 3060 (C-H_{arom}), 1689 (C=O), 1582 (C=N), 1512 (C=C), 1124 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm):
1.95 (s, 2H, NH_2), 2.34 (s, 3H, -CH_3), 5.16 (s, 1H,
$CH_{pyrimidine}$), 5.87 (s, 1H, -N**H**NH_2), 6.91 (s, 1H, NH-C-Ph),
7.30-7.89 (m, 10H, Ar-H), 9.03 (s, 1H, N**H**-C-CH_3). ^{13}C
NMR (100 MHz, DMSO-*d6*, δ ppm): 17.9 (-CH_3), 50.6 (-
$CH_{pyrimidine}$), 123.3 (-$CH_{pyrazole}$), 118.5-149.1 (Ar-C), 150.3 (C=O, NHCONH), 166.2 (C=O). LCMS (ESI) *m/z*: 406.16 $[M]^+$. Anal. calcd. for $C_{21}H_{19}FN_6O_2$: C, 62.06; H, 4.71; N,
20.68. Found: C, 62.00; H, 4.62; N, 20.73 %.

General procedure of synthesis of 4-(3-(4-fluorophenyl)-1-phe- nyl-1*H*-pyr-azol-4-yl)-6-methyl-5-(5-aryl-1,3,4-oxadiazol-2-yl)- 3,4-dihyd-ropyrimidin-2(1*H*)-ones (3a-o)

Compound **2** (0.01 mol) with various derivatives of aromatic acids (0.01 mol) were dissolved and stirred in one pot having phosphoryl chloride ($POCl_3$) (20 mL). The mixture was refluxed at 80 °C for 6 h. After completion of the reaction (TLC), the mixture was slowly quenched on crushed ice. The precipitates were filtered, washed with $NaHCO_3$ to remove excess $POCl_3$ trace followed by water, dried and recrystallized from ethanol (95 %) to furnished final compounds.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-phenyl-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin-2(1*H*)- one (3a)

Yield: 71 %, m.p. 241-242 ºC. IR (KBr): 3223 (NH), 3061
(C-H_{arom}), 2983 (H-C=C<), 2848 (C-H, CH_3), 1685 (C=O),
1598 (C=N), 1527 (C=C), 1281 (C-O-C), 1122 (C-F) cm^{-1}.
^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.36 (s, 3H, -CH_3),
5.18 (s, 1H, $CH_{pyrimidine}$), 6.88 (s, 1H, NH-C-Ph), 7.28-8.06
(m, 14H, Ar-H), 8.14 (s, 1H, $CH_{pyrazole}$), 9.10 (s, 1H, NH-C- CH_3). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 15.1 (-CH_3),
53.6 ($C_{pyrimidine}$), 123.2 ($C_{pyrazole}$), 113.5-149.5 (Ar-C), 150.4
(C=O), 160.3, 164.1 ($C_{oxadiazole}$), 161.6 (C-F). LCMS (ESI) *m/z*: 492.17 $[M]^+$. Anal. calcd. for $C_{29}H_{21}FN_6O_2$: C, 68.28; H, 4.30; N, 17.06. Found: C, 68.19; H, 4.41; N, 17.11 %.

5-(5-(2-Chlorophenyl)-1,3,4-oxadiazol-2-yl)-4-(3-(4-fluorophe- nyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-3,4-dihydropyrimid- in-2(1*H*)-one (3b)

Yield: 65 %, m.p. 218-220 ºC. IR (KBr): 3221 (NH), 3062
(C-H_{arom}), 2981 (H-C=C<), 2850 (C-H, CH_3), 1691 (C=O),
1597 (C=N), 1514 (C=C), 1288 (C-O-C), 1107 (C-F), 754
(C-Cl) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.28 (s,
3H, -CH_3), 5.18 (s, 1H, $CH_{pyrimidine}$), 6.89 (s, 1H, NH-C-Ph),
7.28-8.20 (m, 13H, Ar-H), 8.28 (s, 1H, $CH_{pyrazole}$), 9.16 (s,
1H, N**H**-C-CH_3). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm):
15.2 (CH_3), 53.5 ($C_{pyrimidine}$), 123.6 ($C_{pyrazole}$), 135.3 (C-Cl),
113.2-149.7 (Ar-C), 150.6 (C=O), 160.1, 164.4 ($C_{oxadiazole}$),
161.4 (C-F). LCMS (ESI) *m/z*: 526.13 $[M]^+$. Anal. calcd. for

C28H20ClFN6O2: C, 68.82; H, 3.83; N, 15.95. Found: C,
63.79; H, 3.85; N, 15.93 %.

5-(5-(3-Chlorophenyl)-1,3,4-oxadiazol-2-yl)-4-(3-(4-fluorophe- nyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-3,4-dihydropyrimi- din-2(1*H*)-one (3c)
Yield: 59 %, m.p. 186-188 ºC. IR (KBr): 3222 (NH), 3063
(C-Harom), 2980 (H-C=C<), 2852 (C-H, CH3), 1691 (C=O),
1599 (C=N), 1517 (C=C), 1280 (C-O-C), 1110 (C-F), 754
(C-Cl) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, *δ* ppm): 2.30 (s,
3H, -CH3), 5.16 (s, 1H, CHpyrimidine), 6.85 (s, 1H, NH-C-Ph),
7.29-8.16 (m, 13H, Ar-H), 8.24 (s, 1H, CHpyrazole), 9.15 (s,
1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, *δ* ppm):
15.0 (CH3), 53.3 (Cpyrimidine), 123.4 (Cpyrazole), 135.2 (C-Cl),
113.3-149.5 (Ar-C), 150.7 (C=O), 160.3, 164.6 (Coxadiazole),
161.2 (C-F). LCMS (ESI) *m/z*: 526.13 $[M]^+$. Anal. calcd. for C28H20ClFN6O2: C, 68.82; H, 3.83; N, 15.95. Found: C,
63.90; H, 3.80; N, 15.85 %.

5-(5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl)-4-(3-(4-fluorophe- nyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-3,4-dihydropyrimi- din-2(1*H*)-one (3d)
Yield: 63 %, m.p. 225-227 ºC. IR (KBr): 3293 (NH), 3066
(C-Harom), 2978 (H-C=C<), 2929 (C-H, CH3), 1680 (C=O),
1591 (C=N), 1504 (C=C), 1219 (C-O-C), 1155 (C-F), 752
(C-Cl) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, *δ* ppm): 2.31 (s,
3H, CH3), 5.26 (s, 1H, CHpyrimidine), 6.82 (s, 1H, NH-C-Ph),
7.20-8.05 (m, 13H, Ar-H), 8.16 (s, 1H, CHpyrazole), 9.04 (s,
1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, *δ* ppm):
15.3 (CH3), 53.9 (Cpyrimidine), 123.8 (Cpyrazole), 135.6 (C-Cl),
113.0-149.7 (Ar-C), 150.5 (C=O), 160.6, 164.4 (Coxadiazole),
161.7 (C-F). LCMS (ESI) *m/z*: 526.13 $[M]^+$. Anal. calcd. for C28H20ClFN6O2: C, 68.82; H, 3.83; N, 15.95. Found: C,
63.75; H, 3.86; N, 15.89 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-(2-nitrophenyl)-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin- 2(1*H*)-one (3e)
Yield: 58 %, m.p. 233-235 ºC. IR (KBr): 3224 (NH), 3063
(C-Harom), 2981 (H-C=C<), 2862 (C-H, CH3), 1687 (C=O),
1606 (C=N), 1531 (C=C), 1508 (-N=O), 1234 (C-O-C),
1150 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, *δ* ppm):
2.37 (s, 3H, CH3), 5.20 (s, 1H, CHpyrimidine), 6.85 (s, 1H, NH-
C-Ph), 7.22-8.15 (m, 13H, Ar-H), 8.20 (s, 1H, CHpyrazole),
9.04 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, *δ*
ppm): 15.2 (CH3), 54.0 (Cpyrimidine), 122.9 (Cpyrazole), 113.0-
149.7 (Ar-C), 147.3 (C-NO2), 150.4 (C=O), 160.2, 164.1
(Coxadiazole), 161.5 (C-F). LCMS (ESI) *m/z*: 537.16 $[M]^+$. Anal. calcd. for C28H20FN7O4: C, 62.57; H, 3.75; N, 18.24. Found: C, 62.53; H, 3.69; N, 18.21 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-(3-nitrophenyl)-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin- 2(1*H*)-one (3f)
Yield: 60 %, m.p. 250-252 ºC. IR (KBr): 3221 (NH), 3060
(C-Harom), 2985 (H-C=C<), 2854 (C-H, CH3), 1680 (C=O),
1603 (C=N), 1533 (C=C), 1507 (-N=O), 1231 (C-O-C),

1155 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm):
(s, 3H, CH3), 5.23 (s, 1H, CHpyrimidine), 6.86 (s, 1H, NH-
C-Ph), 7.20-8.21 (m, 13H, Ar-H), 8.29 (s, 1H, CHpyrazole),
9.08 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, δ
ppm): 15.1 (CH3), 54.4 (Cpyrimidine), 123.1 (Cpyrazole), 113.4-
149.9 (Ar-C), 147.6 (C-NO2), 150.5 (C=O), 160.1, 164.6
(Coxadiazole), 161.3 (C-F). LCMS (ESI) *m/z*:
537.10 $[M]^{+}$. Anal. calcd. for C28H20FN7O4: C, 62.57; H, 3.75; N, 18.24. Found: C, 62.52; H, 3.61; N, 18.20 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin- 2(1*H*)-one (3g)

Yield: 66 %, m.p. 269-271 ºC. IR (KBr): 3211 (NH), 3059
(C-Harom), 2980 (H-C=C<), 2848 (C-H, CH3), 1693 (C=O),
1598 (C=N), 1527 (C=C), 1504 (N=O), 1284 (C-O-C), 1157
(C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.40 (s,
3H, CH3), 5.21 (s, 1H, CHpyrimidine), 6.80 (s, 1H, NH-C-Ph),
7.29-8.23 (m, 13H, Ar-H), 8.31 (s, 1H, CHpyrazole), 9.24 (s,
1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm):
15.7 (CH3), 54.7 (Cpyrimidine), 123.4 (Cpyrazole), 113.2-149.2
(Ar-C), 147.1 (C-NO2), 150.6 (C=O), 160.4, 164.9
(Coxadiazole), 161.6 (C-F). LCMS (ESI) *m/z*:
537.13 $[M]^{+}$. Anal. calcd. for C28H20FN7O4: C, 62.57; H, 3.75; N, 18.24. Found: C, 62.62; H, 3.78; N, 18.29 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-5-(5-(2-hyd- roxyphenyl)-1,3,4-oxadiazol-2-yl)-6-methyl-3,4-dihydropyri- midin-2(1*H*)-one (3h)

Yield: 68 %, m.p. 179-181 ºC. IR (KBr): 3409 (OH), 3216
(NH), 3062 (C-Harom), 2984 (H-C=C<), 2845 (C-H, CH3),
1697 (C=O), 1602 (C=N), 1525 (C=C), 1280 (C-O-C), 1151
(C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.35 (s,
3H, CH3), 5.22 (s, 1H, CHpyrimidine), 6.82 (s, 1H, NH-C-Ph),
7.02-8.07 (m, 13H, Ar-H), 8.18 (s, 1H, CHpyrazole), 9.16 (s,
1H, N**H**-C-CH3), 9.20 (s, 1H, OH). ^{13}C NMR (100 MHz,
DMSO-*d6*, δ ppm): 15.0 (CH3), 53.4 (Cpyrimidine), 123.2
(Cpyrazole), 113.2-149.7 (Ar-C), 150.1 (C=O), 157.3 (C-OH),
, 164.4 (Coxadiazole), 161.8 (C-F). LCMS (ESI) *m/z*:
508.16 $[M]^{+}$. Anal. calcd. for C28H21FN6O3: C, 66.14; H,
4.16; N, 16.53. Found: C, 66.23; H, 4.12; N, 16.58 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-5-(5-(3-hyd- roxyphenyl)-1,3,4-oxadiazol-2-yl)-6-methyl-3,4-dihydropyri- midin-2(1*H*)-one (3i)

Yield: 57 %, m.p. 271-273 ºC. IR (KBr): 3412 (OH), 3217
(NH), 3064 (C-Harom), 2987 (H-C=C<), 2848 (C-H, CH3),
1698 (C=O), 1609 (C=N), 1528 (C=C), 1252 (C-O-C), 1151
(C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.34 (s,
3H, CH3), 5.19 (s, 1H, CHpyrimidine), 6.80 (s, 1H, NH-C-Ph),
6.99-8.14 (m, 13H, Ar-H), 8.20 (s, 1H, CHpyrazole), 9.14 (s,
1H, N**H**-C-CH3), 9.19 (s, 1H, OH). ^{13}C NMR (100 MHz,
DMSO-*d6*, δ ppm): 15.3 (CH3), 53.1

(Cpyrimidine), 123.4
(Cpyrazole), 113.0-149.8 (Ar-C), 150.4 (C=O), 157.6 (C-OH),
, 164.3 (Coxadiazole), 161.2 (C-F). LCMS (ESI) *m/z*:
508.16 $[M]^+$. Anal. calcd. for C28H21FN6O3: C, 66.14; H,
4.16; N, 16.53. Found: C, 66.26; H, 4.20; N, 16.61 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-5-(5-(4-hyd- roxyphenyl)-1,3,4-oxadiazol-2-yl)-6-methyl-3,4-dihydropyri- midin-2(1*H*)-one (3j)

Yield: 73 %, m.p. 237-239 ºC. IR (KBr): 3418 (OH), 3219
(NH), 3062 (C-Harom), 2981 (H-C=C<), 2853 (C-H, CH3),
1692 (C=O), 1605 (C=N), 1526 (C=C), 1278 (C-O-C), 1160
(C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.37 (s,
3H, CH3), 5.22 (s, 1H, CHpyrimidine), 6.83 (s, 1H, NH-C-Ph),
6.96-8.17 (m, 13H, Ar-H), 8.21 (s, 1H, CHpyrazole), 9.16 (s,
1H, N**H**-C-CH3), 9.20 (s, 1H, OH). ^{13}C NMR (100 MHz,
DMSO-*d6*, δ ppm): 15.0 (CH3), 53.3 (Cpyrimidine), 123.0
(Cpyrazole), 113.6-149.9 (Ar-C), 150.6 (C=O), 158.4 (C-OH),
160.6, 164.7 (Coxadiazole), 161.8 (C-F). LCMS (ESI) *m/z*:
508.16 $[M]^+$. Anal. calcd. for C28H21FN6O3: C, 66.14; H,
4.16; N, 16.53. Found: C, 66.19; H, 4.22; N, 16.60 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-5-(5-(4-meth- oxyphenyl)-1,3,4-oxadiazol-2-yl)-6-methyl-3,4-dihydropyrimi- din-2(1*H*)-one (3k)

Yield: 64 %, m.p. 184-186 ºC. IR (KBr): 3216 (NH), 3063
(C-Harom), 2985 (H-C=C<), 2944 (OCH3), 2850 (C-H, CH3),
1698 (C=O), 1606 (C=N), 1527 (C=C), 1281 (C-O-C), 1163
(C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.39 (s,
3H, CH3), 3.60 (s, 3H, OCH3), 5.19 (s, 1H, CHpyrimidine), 6.84
(s, 1H, NH-C-Ph), 7.01-8.14 (m, 13H, Ar-H), 8.20 (s, 1H, CHpyrazole), 9.17 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100 MHz,
DMSO-*d6*, δ ppm): 15.2 (CH3), 53.6 (Cpyrimidine), 55.6
(OCH3), 123.7 (Cpyrazole), 113.4-149.8 (Ar-C), 150.1 (C=O),
160.1, 164.5 (Coxadiazole), 161.9 (C-F). LCMS (ESI) *m/z*:
522.17 $[M]^+$. Anal. calcd. for C29H23FN6O3: C, 66.66; H,
4.44; N, 16.08. Found: C, 66.71; H, 4.53; N, 16.17 %.

4-(3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-*p*-tolyl-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin-2(1*H*)-one (3l)

Yield: 74 %, m.p. 213-215 ºC. IR (KBr): 3219 (NH), 3068
(C-Harom), 2986 (H-C=C<), 2856, 2860 (C-H, CH3), 1701
(C=O), 1602 (C=N), 1531 (C=C), 1284 (C-O-C), 1165 (C- F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm): 2.37 (s, 3H,
CH3Pyrimidine), 2.44 (s, 3H, CH3arom), 5.21 (s, 1H, CHpyrimidine),
6.86 (s, 1H, NH-C-Ph), 7.07-8.18 (m, 13H, Ar-H), 8.22 (s,
1H, CHpyrazole), 9.18 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100
MHz, DMSO-*d6*, δ ppm): 15.0 (CH3Pyrimidine), 21.2 (CH3arom),
53.2 (Cpyrimidine), 123.2 (Cpyrazole), 113.1-149.7 (Ar-C), 150.2
(C=O), 160.2, 164.2 (Coxadiazole), 161.4 (C-F). LCMS (ESI)
m/z: 506.19 $[M]^+$. Anal. calcd. for C29H23FN6O2: C, 66.76; H,
4.58; N, 16.59. Found: C, 66.77; H, 4.52; N, 16.68 %.

***N*-((5-(4-(3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6- methyl-2-oxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1,3,4-oxa- diazol-2-yl)methyl)benzamide (3m)**

Yield: 61 %, m.p. 227-229 ºC. IR (KBr): 3221

(NH), 3061
(C-Harom), 2984 (H-C=C<), 2921 (C-H, CH2), 2852 (C-H,
CH3), 1703 (C=O), 1605 (C=N), 1528 (C=C), 1281 (C-O-C), 1160 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm):
(s, 3H, CH3), 4.06 (s, 2H, CH2), 5.25 (s, 1H,
CHpyrimidine), 6.87 (s, 1H, NH-C-Ph), 7.10-8.20 (m, 14H, Ar-
H), 8.24 (s, 1H, CHpyrazole), 8.68 (s, 1H, NHCO), 9.17 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 15.4
(CH3), 43.4 (CH2), 53.5 (Cpyrimidine), 123.6 (Cpyrazole), 113.0-
149.1 (Ar-C), 150.7 (C=O), 160.4, 164.3 (Coxadiazole), 161.5
(C-F), 167.5 (NHCO). LCMS (ESI) *m/z*: 549.19 $[M]^{+}$. Anal. calcd. for C30H24FN7O3: C, 66.57; H, 4.40; N, 17.84. Found: C, 66.55; H, 4.46; N, 17.88 %.

5-(5-Benzyl-1,3,4-oxadiazol-2-yl)-4-(3-(4-fluorophenyl)-1- phenyl-1*H*-pyrazol-4-yl)-6-methyl-3,4-dihydropyrimidin- 2(1*H*)-one (3n)

Yield: 62 %, m.p. 195-197 ºC. IR (KBr): 3219 (NH), 3066
(C-Harom), 2987 (H-C=C<), 2923 (C-H, CH2), 2854 (C-H,
CH3), 1705 (C=O), 1604 (C=N), 1531 (C=C), 1284 (C-O-C), 1166 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm):
2.34 (s, 3H, CH3), 4.01 (s, 2H, CH2), 5.22 (s, 1H,
CHpyrimidine), 6.86 (s, 1H, NH-C-Ph), 7.12-8.19 (m, 14H, Ar-
H), 8.22 (s, 1H, CHpyrazole), 9.15 (s, 1H, N**H**-C-CH3). ^{13}C
NMR (100 MHz, DMSO-*d6*, δ ppm): 15.1 (CH3), 31.2 (CH2),
53.7 (Cpyrimidine), 123.3 (Cpyrazole), 113.4-149.6 (Ar-C), 150.4
(C=O), 160.1, 164.7 (Coxadiazole), 161.7 (C-F). LCMS (ESI)
m/z: 506.19 $[M]^{+}$. Anal. calcd. for C29H23FN6O2: C, 68.76; H,
4.58; N, 16.59. Found: C, 68.85; H, 4.65; N, 16.62 %.

4-(3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-6-methyl-5- (5-styryl-1,3,4-oxadiazol-2-yl)-3,4-dihydropyrimidin-2(1*H*)-one (3o)

Yield: 72 %, m.p. 275-277 ºC. IR (KBr): 3224 (NH), 3151
(C-Harom), 3024 (H-C=C-H), 2980 (H-C=C<), 2920 (C-H,
CH3), 1708 (C=O), 1597 (C=N), 1500 (C=C), 1217 (C-O-C), 1178 (C-F) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-*d6*, δ ppm):
2.26 (s, 3H, CH3), 5.44 (s, 1H, CHpyrimidine), 6.42 (d, 1H,
CH=C**H**arom), 6.46 (d, 1H, CH=C**H**oxadiazole), 7.06 (s, 1H, NH-C-Ph), 7.13-7.97 (m, 14H, Ar-H), 8.00 (s, 1H, CHpyrazole), 9.21 (s, 1H, N**H**-C-CH3). ^{13}C NMR (100 MHz,
DMSO-*d6*, δ ppm): 15.1 (CH3), 53.4 (Cpyrimidine), 123.1
(Cpyrazole), 123.1 (CH=CHoxadiazole), 133.1 (CH=CHarom),
113.4-149.8 (Ar-C), 150.1 (C=O), 159.9, 164.0 (Coxadiazole),
161.2 (C-F). LCMS (ESI) *m/z*: 518.19 $[M]^{+}$. Anal. calcd. for C30H23FN6O2: C, 69.49; H, 4.47; N, 16.21. Found: C, 69.45;
H, 4.44; N, 16.32 %.

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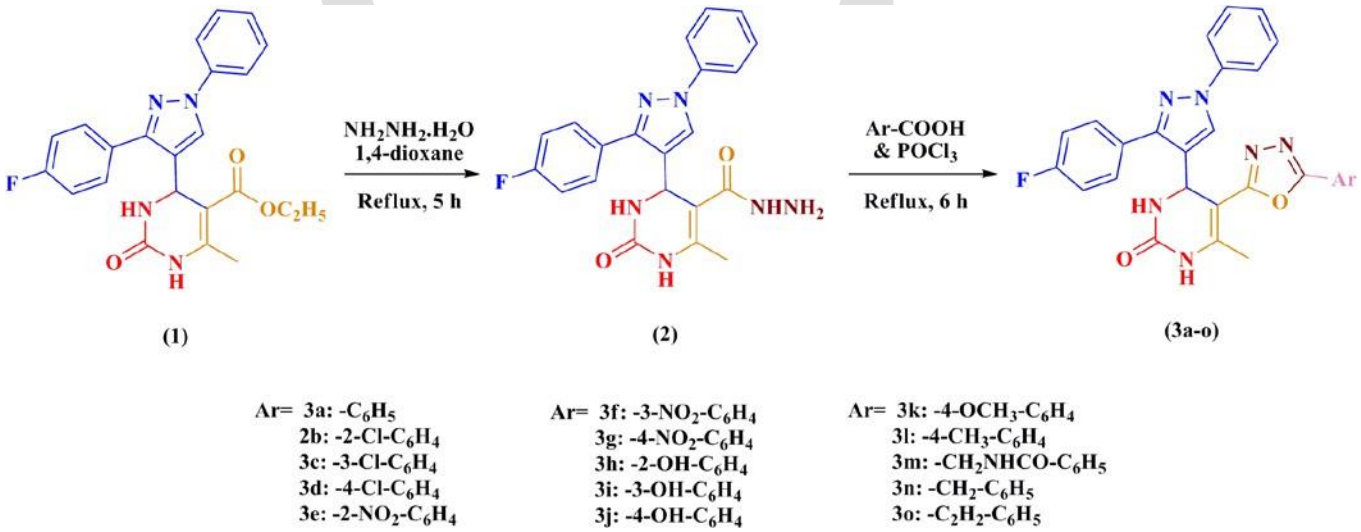
RESULTS AND DISCUSSION

Synthesis of compounds of interest is shown in Scheme 1. Second, hydrazine hydrate (NH2-NH2) was added to the mixture after the diaryl-pyrazole-4-carbaldehyde step in the famous Biginelli reaction, which yielded compound 2. The final compounds were produced by treating this adduct with various aryl acid derivatives in a one-pot reaction. The chemical compound 4-(3-(4-fluorophenyl)The compound is named phenyl-1-hydrazolyl.6 -methyl-5-(5-aryl-1,3,4-oxadiazol-2-yl)2, 1-hydropyrimidin-2-one hydrogen bonded to C=Oand ones from 3a to o.

Prior to testing the synthetic compounds for antibacterial activity in vitro, they underwent spectroscopic characterization using established methods. Compound 3a-o's infrared spectra revealed a carbonyl group absorption band at 1710-1680 cm-1 and a secondary amine absorption band at 3293-3212 cm-1. At 3151-3058, 2998-2978, and 2929-2845 cm-1, respectively, vibrations were detected that correspond to the aromatic ring's C-H stretching, H-C=C<, and -CH3. The stretching of the aromatic ring is shown by the absorption bands at 1609–1592, 1533–1500 cm-1, and 1289–1217 cm-1, while the stretching of the oxadiazole ring is indicated by the bands at 1289–1217 cm-1. The three singlet peaks seen in 1H NMR at δ = 2.26-2.40, 5.17-5.45, and 9.04-9.24 ppm, respectively, were caused by three protons: one from the methyl group, one from the -CH of the pyrimidine ring, and one from the -NH of the pyrimidine ring (-NH-C-CH3). It was one proton of the -NH group in the pyrimidine ring (-NH-C-Ph) that caused the singlet signal at δ = 6.80-7.06 ppm to arise. A distinct signal at δ = 150.2-151.3 ppm, attributed to the carbonyl carbon of the pyrimidine scaffold, and an additional signal at δ = 15.0-15.2 ppm, attributed to the carbon of the methyl group, were seen in the 13C NMR spectrum of compound 3a-o. In addition, the mass spectra confirmed the predicted chemical structure and molecular weight by showing a peak for a molecular ion with the formula 3a-o in addition to other fragment peaks.



Scheme 1. Synthetic pathway of novel compounds **3a-o**

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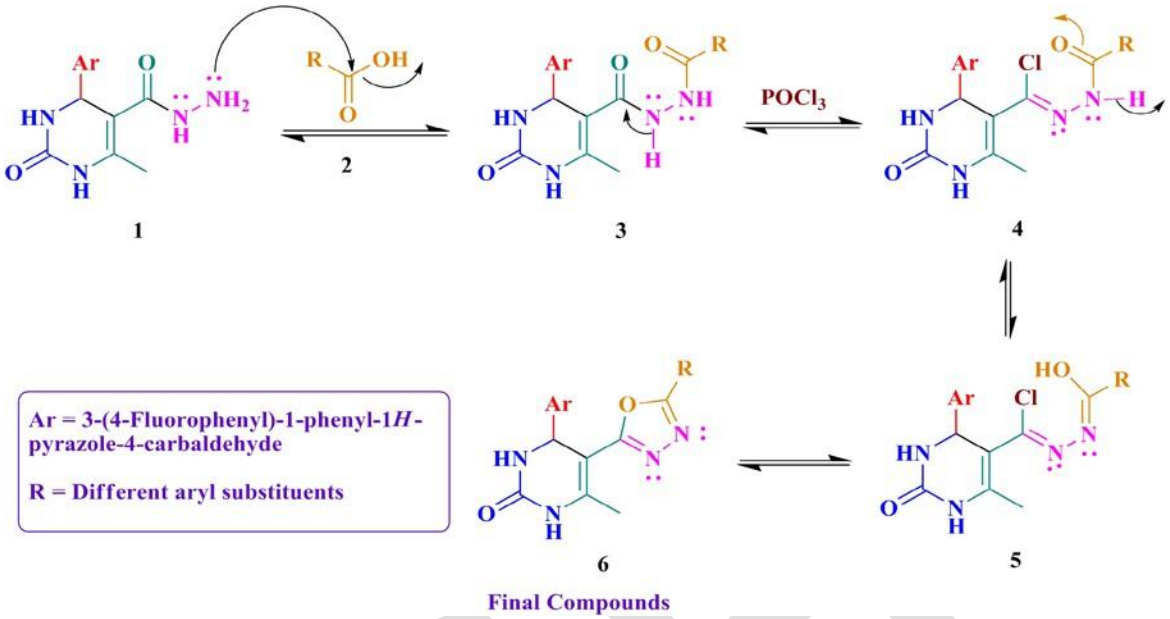

Figure 1. Plausible mechanistic pathway of synthesized analogs

A plausible mechanistic path for compounds **3a-o** is suggested in Figure **1**. Biginelli hydrazide **(1)** was transformed to targeted compounds **(6)** by intermolecular nucleophilic attack on the carbonyl carbon of different aromatic acids **(2)** followed by the cyclocondensation (removal of HCl) **(5)** in the presence of phosphorus oxychloride ($POCl_3$).

Antimicrobial activity

Amongst the synthesized compounds **3a-o**, several compounds revealed the antimicrobial influence that ranged from good to excellent. On the basis of antibacterial screening results given in Table 1, compounds **3j** (-4-OH- C_6H_4), **3k** (-4-OCH_3-C_6H_4) and **3l** (-4-CH_3-C_6H_4) displayed noteworthy antibacterial activities against *E. coli*, *P. aeruginosa*, *S. aureus*, *S. pyogenes* compared to chloramphenicol and Ciprofloxacin used as standard drugs. MIC values of antifungal activity were determined by means of conventional broth microdilution bioassay method using Nystatin and Griseofulvin as a reference standard.[24] Compounds **3h** (-2-OH-C_6H_4) and **3l** (-4-CH_3-C_6H_4) unveiled remarkable inhibitory effect at MIC = 12.5 µg mL^{-1} against selected fungal strains.

Antitubercular and cytotoxic activity

Synthesized oxadiazole hybrid molecules **3a-o** were screened for their *in vitro* antitubercular activity at 6.25 µg mL^{-1} against *Mycobacterium tuberculosis* H37Rv strain in BACTEC 12B medium using the microplate alamar blue assay (MABA).[25] In an initial screen, the compounds which shown more than or equal to 90 % inhibition were retested at and below 6.25 µg mL^{-1} by using 2-fold dilution to determine the definite MIC. In preliminary *in vitro* screening, compounds **3d**, **3h, 3j**, **3k** and **3l** inhibited Mtb in the range of 92-98 %. In secondary level screening, two compounds **3j** (-4-OH-C_6H_4) and **3l** (-4-CH_3-C_6H_4) inhibited Mtb with MIC of 0.03 µg mL^{-1} correspond to the same MIC as the reference standard isoniazid.

Compounds revealing comparatively low MICs were tested for cytotoxicity (IC_{50}) in VERO cell lines. Their selectivity index (SI) was calculated as per the following formula IC_{50}/MIC. The compounds **3h**, **3j** and **3l** were somehow less toxic than **3d** and **3k**. Basically, the compounds with MIC≤6.25 µg mL^{-1} and SI≥10 are remarkable compounds and MIC≤1 µg mL^{-1} in the newly synthesized compound may be considered as excellent leadership,

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which makes compounds **3j** and **3l** promising bioactive molecules for future research. The results of the antitubercular studies, actual IC50 and SI of tested compounds were reported in Table 2.

Determination of 50 % IC50 in VERO cells (Cytotoxicity assay)

At doses below or equivalent to 62.5 µg mL-1, or 10 times the MIC for M. tuberculosis H37Rv, compounds were examined for cytotoxicity (IC50) in VERO cells. The Promega CellTiter 96 Non-radioactive Cell Proliferation Assay was used to measure cellular conversion of MTT into a formazan product after 72 hours of exposure, which is a measure of viability. Additionally, the Selectivity Index (SI) was calculated as IC50 divided by MIC. A SI greater than 10 was deemed statistically significant.

Structure-activity relationship study

Substances were tested for cytotoxicity (IC50) in VERO cells at doses less than or equal to 62.5 µg mL-1, which is 10 times the minimum inhibitory concentration (MIC) for Mycobacterium tuberculosis H37Rv. For the purpose of determining cell viability, the Promega CellTiter 96 Non-radioactive Cell Proliferation Assay was used to assess the amount of MTT converted into a formazan product after 72 hours of exposure. One more thing: we divided the IC50 by the MIC to get the Selectivity Index (SI). Statistical significance was determined by a SI higher than 10.

No.	-Ar	MINIMUM INHIBITORY CONCENTRATIONS, MIC, in µg mL^{-1}						
		Gram-negative		Gram-positive		Fungi		
		E.C.[a]	*P.A.*[b]	*S.A.*[c]	*S.P.*[d]	*C.A.*[e]	*A.N.*[f]	*A.C.*[g]
3a	-C6H5	500	250	500	250	500	N.A.[h]	N.A.
3b	-2-Cl-C6H4	125	250	500	100	500	NA.	NA.
3c	-3-Cl-C6H4	100	100	100	500	NA.	NA.	500
3d	-4-Cl-C6H4	25	62.5	25	100	500	NA.	NA.
3e	-2-NO2-C6H4	1000	500	500	500	NA.	250	NA.
3f	-3-NO2-C6H4	1000	1000	500	500	250	100	250
3g	-4-NO2-C6H4	500	100	1000	1000	500	NA.	NA.
3h	-2-OH-C6H4	100	1000	1000	500	NA.	100	12.5
3i	-3-OH-C6H4	1000	100	500	50	NA.	1000	NA.
3j	-4-OH-C6H4	12.5	25	1000	100	1000	1000	100
3k	-4-OCH3-C6H4	100	250	500	12.5	50	1000	1000
3l	-4-CH3-C6H4	500	500	25	1000	100	12.5	NA.
3m	-CH2NHCOC6H5	1000	1000	250	500	1000	NA.	50
3n	-CH2-C6H5	500	1000	100	500	NA.	50	1000
3o	-C2H2-C6H5	1000	500	250	1000	1000	500	1000
S.d.1[i]	Chloramphenicol	50	50	50	50	-	-	-
S.d.2	Ciprofloxacin	25	25	50	50	-	-	-
S.d.3	Nystatin	-	-	-	-	100	100	100

S.d. 4	Griseofulvin	-	-	-	-	500	100	100

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Table 1. Antimicrobial screening of the compounds **3a-o**.

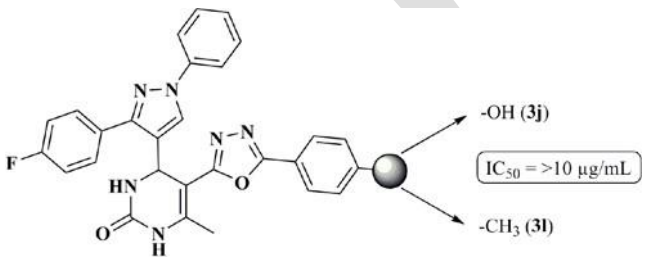
[a]*E.C.: Escherichia coli* MTCC 443; [b]*P.A.:Pseudomonas aeruginosa* MTCC 1688, [c]*S.A.: Staphylococcus aureus* MTCC 96; [d]*S.P.: Staphylococcus pyogenes* MTCC 442; [e]*C.A.: Candida albicans* MTCC 227; [f]*A.N.: Aspergillus niger* MTCC 282; [g]*A.C.: Aspergillus clavatus* MTCC 1323; [h]N.A.: No activity; [i]S.d.: Standard drug.

Table 2. *In vitro* antitubercular screening data of oxadiazole analogs **3a-o**.

No.	-Ar	% Inhibition, at 6.25 µg mL^{-1}	MIC[a], µg mL^{-1}	IC$_{50}$, VERO cells	SI[c]=IC50/MIC
3a	-C$_6$H$_5$	65	n.d.[f]	n.d.	n.d.
3b	-2-ClC$_6$H$_4$	55	n.d.	n.d.	n.d.
3c	-3-ClC$_6$H$_4$	52	n.d.	n.d.	n.d.
3d	-4-ClC$_6$H$_4$	92	6.25	7.2	1.15
3e	-2-NO$_2$C$_6$H$_4$	48	n.d.	n.d.	n.d.
3f	-3-NO$_2$C$_6$H$_4$	71	n.d.	n.d.	n.d.
3g	-4-NO$_2$C$_6$H$_4$	62	n.d.	n.d.	n.d.
3h	-2-HOC$_6$H$_4$	93	3.13	>10	>3.19
3i	-3-HOC$_6$H$_4$	82	n.d.	n.d.	n.d.
3j	-4-HOC$_6$H$_4$	98	0.03	>10	333
3k	-4-MeOC$_6$H$_4$	96	1.56	8.9	5.70
3l	-4-CH$_3$-C$_6$H$_4$	97	0.03	>10	333
3m	-CH$_2$NHCOC$_6$H$_5$	81	n.d.	n.d.	n.d.
3n	-CH$_2$C$_6$H$_5$	73	n.d.	n.d.	n.d.
3o	-C$_2$H$_2$C$_6$H$_5$	84	n.d	n.d.	n.d.
R.S.[a]	INH[e]	99	0.03	-	-

[a]Minimum inhibitory concentration against H37Rv strain of *M. tuberculosis* (µg mL^{-1}). [b]Measurement of cytotoxicity in VERO cells: 50% inhibitory concentrations (µg mL^{-1}). [c]Selectivity index (*in vitro*): IC50 in VERO cells/MIC against *M. tuberculosis*. [d]R.S.: Reference Standard; [e]INH: Isoniazid; [f]n.d.: Not determined.

Compounds **3h**, **3j, 3k** and **3l**, substituted with inductively electron-donating groups like methyl, methoxy (on *para*) and hydroxyl (on *ortho* and *para*), showed the maximum inhibitory antimicrobial as well as antitubercular influence



CONCLUSION

An important goal of this study was to create new structural hybrids of DHPMs and pyrazole called 1,3,4-oxadiazole; these compounds have the potential to be powerful antibacterial and antitubercular medicines. Biological activity leads us to believe that these compounds' structural and electrical diversity impact their activity. The most effective antimicrobials and antitubercular

candidates were scaffolds 3h, 3j, 3k, and 3l that included an electron-donating group like -OH, -OCH3, or -CH3. In addition, the compounds with the highest activity, 3j and 3l, were transported with a moderate level of cytotoxicity. So, this hybrid nucleus might provide a relatively easy way to novel antibacterial and antitubercular scaffolds.

REFERENCES

- International Journal of Antimicrobial Agents, 2011, 37, 2-9 (Moellering Jr., R. C., 2011). Journal Article: 10.1016/j.ijantimicag.2010.08.018
  Dalton, V., and Barry, C. E. Bioorg. Med. Chem. Lett., 2013, 23(17), 4741-4750, provides a medicinal chemist's approach to the problems associated with optimising leads for TB. Publication Date: July 6, 2013
  Journal of Heterocyclic Chemistry, 2020, 1023-1033, Safari, S., Ghavimi, R., Razzaghi-Asl, N., and Sepehri, S., Synthesis, biological assessment, and molecular docking investigation of dihydropyrimidine derivatives as prospective medicines against cancer. The citation for the article is 10.1002/jhet.3822.
  4-Kappe, C. O., Shishkin, O. V., Uray, G., and Verdino, P., X-ray structure, conformational analysis, enantioseparation, and determination of absolute configuration of the mitotic kinesin Eg5 inhibitor monastrol: a synthetic and reaction-oriented Biginelli compound, Tetrahedron, 2000, 56, 1859–1862. Publication: 10.1016/S0040-4020(00)00116-2
  With the help of Salunkhe, Anbhule, Patil, and M. B. Deshmukh, the authors of this work The antibacterial activity of 2-amino-5-cyano-6-hydroxy-4-aryl pyrimidines and their rapid one-step production, The article is published in the European Journal of Medical Chemistry and has the reference number 44, lines 2651–2654. Reference: 10.1016/j.ejmech.2008.10.018 6.A study was published in the Journal of Biomedical Science in 2010 that described a pyrazole chemical called BPR1P0034 that had strong and selective anti-influenza virus activity. The authors of the study were Shih et al., Chu et al., Reddy et al., Tseng et al., Chen et al., Tang et al., Wu et al., Yeh et al., Chao et al., Hsu et al., Hsieh et al., and Horng et al. URL: 10.1186/1423-0127-17-13(2016)

7“Pyrazole scaffold: a remarkable tool in the development of anticancer agents” (Kumari, H., Saini, D., Jain, S., Jain, N., 2013, 70, 248-258) published in the European Journal of Medical Chemistry. Publication Date: October 10, 2013
In a study conducted by Abdel-Aziz, Abuo-Rahma, and Hassan, the authors were Developing new pyrazole compounds and studying their effects on depression and seizures, published in 2009 in the European Journal of Medical Chemistry, 44, 3480–3487.Published online: 10.1016/j.ejmech.2009.01.032
9The antinociceptive, anti-inflammatory, and antipyretic effects of 1.5-diphenyl-1H-pyrazole-3-carbohydrazide, a new heterocyclic pyrazole derivative, were investigated in a study published in Life Sciences in 2014. The authors of the study were Malvar, Dd. C., Ferreira, R. T., de Castro, R. A., de Castro, L. L., Freitas, A. C. C., Costa, E. A., Florentino, I. F., Mafra, J. C. M., de Souza, G. E. P., and Vanderlinde, F. A. (doi: 10.1016/j.lfs.2013.12.005)
A magnesium chloride catalyst for the synthesis of 1,3,5-trisubstituted pyrazoles was developed by Fatmeh Mirjalili, Bamoniri, Amrollahi, and Emtiazi in 2010. "Discussion of Nanomaterials" (2010, 5, 897-902).Source: http://www.chalcogen.ro/897_Mirjalili.pdf
11The synthesis of pyrazoles and diazepines in an aqueous medium at room temperature: a greener and faster alternative to traditional methods, Polshettiwar and Varma's 2008 article in Tetrahedron Lett., 49, 397–400. Journal Article: 10.1016/j.tetlet.2007.11.017
12Design, synthesis and biological assessment of 1,3,4-oxadiazoles as prospective anti-inflammatory drugs, Med.

Chem. Res., 2017, 26, 190-204, by Iyer, V. B., Gurupadayya, B., Koganti, V. S., Inturi, B., and Chandan, R. S. The article's DOI is 10.1007/s00044-016-1740-6.
13Synthesis, Biological Evaluation and Docking Study of Some Novel Isoxazole Clubbed 1,3,4-Oxadiazoles Derivatives, Med. Chem. Res., 2018, 27, 1283–1291, by Shingare, R. M., Patil, Y. S., Sangshetti, J. N., Patil, R. B., Rajani, D. P., and Madje, B. R. The publication reference is: 10.1007/s00044-018-2148-2.
14"Derivatives of benzimidazole pharmacophore: synthesis, anticonvulsant, antidiabetic and DNA cleavage studies," published in the European Journal of Medical Chemistry in 2010, pages 1753–1759, by Shingalapur, R. V., Hosamani, K. M., Keri, R. S., and Hugar, M. H. 2021-01-07 DOI: 10.1016/j.ejmech.2010.01.007"Molecular properties prediction and synthesis of novel 1,3,4-oxadiazole analogues as potent antimicrobial and antitubercular agents" was published in Bioorg. Med. Chem. Lett. in 2011 and authored by Ahsan, M. J., Samy, J. G., Khalilullah, Nomani, M. S., Saraswat, P., Gaur, R., and Singh, A. 16 DOI: 10.1016/j.bmcl.2011.10.057 18.The chemical synthesis and assessment of the anti-inflammatory and analgesic effects of 3-[(5-substituted-1,3,4-oxadiazol-2-yl-thio)acetyl]-2H-chromen-2-ones was carried out by Ingale, N., Maddi, V., Palkar, M., Ronad, P., Mamledesai, S., Vishwanathswamy, A. H. M., and Satyanarayana, D. Publication: Med. Chem. Res., 2012, 21, 16-26. Article has the DOI: 10.1007/s00044-010-9494-z 17.These authors are associated with the following: Macaev, F., Rusu, G., Pogrebnoi, S., Gudima, A., Stingaci, E., Vlad, L., Shvets, N., Kandemirli, F., Dimoglo, A., Reynolds, R. Bioorg. Med. Chem.,2005, 13, 4842-4850, describes the synthesis of new 5-aryl-2-thio-1,3,4-oxadiazoles and an investigation into their structure-anti-mycobacterial properties. The article's DOI is 10.1016/j.bmc.2005.05.011.With Choudhary, Khan, Rani, and Atta-ur-Rahman, Khan, M. T., and Khan, K. M. Bioorg. Med. Chem., 2005, 13, 3385–3395, Structure–activity interactions of a combinatorial library of 2,5-disubstituted-1,3,4-oxadiazole analogues as tyrosinase inhibitors. Article with the DOI: 10.1016/j.bmc.2005.03.012 19Journal of Organic and Medicinal Chemistry, 2008, 16, 7565–7572; Ke, S., Li, Z., and Qian, X., 1,3,4-Oxadiazole-3(2H)-carboxamide derivatives as a possible new family of monoamine oxidase (MAO) inhibitors: synthesis, assessment, and function of the urea moiety. 20, DOI: 10.1016/j.bmc.2008.07.026}The synthesis and antimicrobial activity of fluorine-containing pyrazole-clubbed dihydropyrimidinones were investigated in a study published in the Indian Journal of Pharmaceuticals by Desai, Vaghani, Patel, and Karkar.

Article cited as Science (2018) 80, 242-252. the following DOI: 10.4172/pharmaceutical-sciences.1000351–21"Synthesis, characterization and antimicrobial screening of thiazole based 1,3,4-oxadiazoles heterocycles" was published in the journal Res. Chem. Intermed. in 2016 and authored by Desai, Bhatt, Dodiya, Karkar, Patel, Bhatt, and Bhatt, M. this article's DOI: 10.1007/s11164-015-25196-0A study was conducted by Desai, N. C., Shihory, N., Bhatt, M., Patel, B., and Karkar, T. to evaluate the antimicrobial properties of certain 1-((1-(1-(1-(1-(1-(1-(1-(1-"H-benzo[d]imidazol-2-yl) ethylidene) amino).(arylidene) amino-6-oxo2,5-dicarbonitriles of 2-oxo-4-phenyl-1,2-dihydropyridine "Synthetic Communications" 2015, 45, 2701–2711. 00397911.2015.1102286 (23).The authors of the article "Novel dihydropyrimidines as a potential new class of antitubercular agents" (Trivedi et al., 2010) include Bhuva, Dholariya, Dodiya, Kataria, and Shah. The article can be found in Bioorg.

Med. Chem. Lett., volume 20, pages 610-6102. Date: 2010-08-24 Publication: BMC Chemistry"Synthesis and antimicrobial activity of novel quinoline derivatives bearing pyrazoline and pyridine analogues," published in Med. Chem. Res. in 2017, pages 109–119, is written by Desai, N. C., Patel, B. Y., and Dave, B. P. 10.1177/s00044-016-1732-6 Online citation