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SYNTHESIS AND ANTIMICROBIAL EVALUATION OF N'-ARYL-3-(4,5-DIPHENYLOXAZOL-2-YL)- PROPANEHYDRAZIDES

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ABSTRACT

A simple, efficient and environmetally benign method was developed towards the synthesis of a series of *N'-aryl-3-(4,5-diphenyloxazol-2-yl)- propanehydrazides* **4a-4j** catalyzed by meglumine. All the substares were obtained in good yields under moderate reaction conditions. The precusor *3-(4,5-diphenyloxazol-2-yl)propanehydrazide* is obtained in excellent yields from *3-(4,5-diphenyl-1,3-oxazol-2-yl) propanoic acid*. All the prepared hydrazones were characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass analysis. Furthermore, the compounds **4a-4j** were also screened for their antimicrobial activity. The anti-microbial activities of the prepared compounds were investigated against four bacterial strains: *Xanthomonas campestris*, *Escherichia coli, Bacillus cereus, Bacillus megaterium* and a fungal strain *Candida albicans*. The biological evaluation studies of these *N'-aryl-3-(4,5-diphenyloxazol-2-yl)- propanehydrazides* revealed that some of these test compounds possess moderate *in vitro* antimicrobial activity.

Keywords: Hydrazones, Anti-microbial activity, Meglumine catalyst.

1. INTRODUCTION

Hydrazone derivatives are a significant class of organic molecules that can be utilized as valuable building blocks for synthesis of bioactive natural products and functional materials [1]. Hydrazone and its derivatives posessing azomethine -NHN=CH- group show a wide range of biological activities [2]. A variety of hydrazone derivatives were screened for potential pharmacological activities which includes anti-inflammatory, analgesic, anti-bacterial, anti-hypertensive, anti-fungal, anti-platelet, anti-cancer, anti-malarial, anti-convulsant, anti-depressant and anti-viral activities [3] have been constructed. Apart from the extensive biological properties they can also combine with other functional groups to provide pharmacologically active molecules. Moreover the presence of azomethine proton (HN-N=CH-) in hydrazones has gained special interest for the development of novel drugs. Some of the hydrazone derivatives like chloropyrrole based aroyl hydrazone reported by Demirbas *et al* [4], 4-bromophenoxy acetic acid hydrazones developed by Raja *et al* [5] and hydrazone Schiff's base derivatives synthesized by Kale *et al* [6] showed potent antimicrobial activity (Fig. 1).

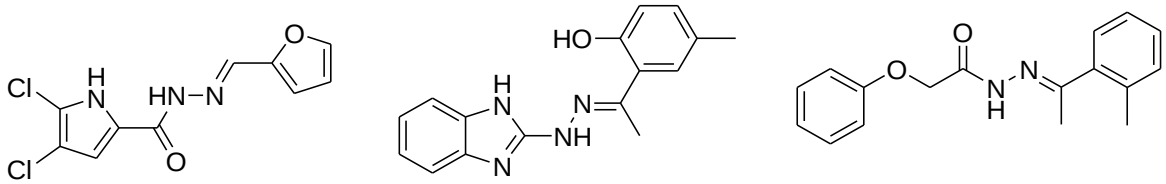


Fig. 1: Some hydrazones with antimicrobial activity

Non-steroidal anti-inflammatory drugs (NSAIDs) are often utilized for the investigation of fever, inflammation and pain. They are frequently used to relieve symptoms of headache, sprains and strains, to reduce longterm pains, flu and arthritis etc. This group of drugs exhibits their pharmacological action *via* inhibition of cyclooxygenase (COX) that catalyzes the conversion of arachidonic acid to the prostaglandins (PGs) [7-9]. COX has been established to occur mainly in two different isoforms, COX-1 and COX-2. In normal tissues, COX-2

is undetectable and selectively induced locally by inflammatory stimuli [10-12]. On the other hand, COX-1 is constitutively normally expressed in most tissues. Some of the NSAIDs with therapeutic interest [13] were shown in below Fig. 2. Recently, synthesis of a series of mefenamic acid (Fig. 2) based acyl hydrazones with potent *in vitro* cytotoxic properties have been reported [14-15]. Similarly, the hydrazones obtained from diclofenac (Fig. 2) were reported to exhibit both *in vivo* and *in vitro* antimycobacterial activities [16].

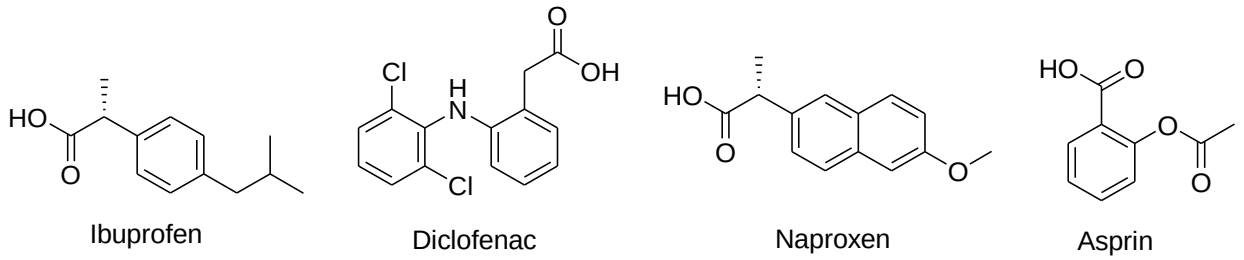


Fig. 2: Some Non-steroidal anti-inflammatory drugs

In view of pharmalogical importace of hydrazones various methods have been developed towards the construction of hydrazones among which the classical approach is the condensation of carbonyl compounds and hydrazides. But this widely used method requires harsh dehydrating conditions [17]. Apart from it few acid catalysts like glacial acetic acid [18], polystyrene sulfonic acid [19], zeolites [20] have been developed to promote this reaction. Additionally, ultrasonic irradiation [21], microwave irradiation [22] or by kneading ball-milling technique [23] were also developed to perform this reaction. Despite the efficiency of these methods for the construction of hydrazone derivatives, some of these methods suffer from disadvantages like, the use of volatile organic solvents, low yields, long reaction times, high temperature, over oxidation products, tedious purification processes, the lack of generality etc. Especially, under acidic conditions deprotection of many protecting groups occurs easily.

Considering these broad range of pharmacological applications of hydrazones, NSAIDs and in continuation of the previous efforts to develop biologically potent heterocyles, we wish to prepare the 3-(4,5-diphenyl-1,3-oxazol-2-yl) propanoic acid (oxaprozin) based hydrazone scaffolds and to screen for their antimicrobial properties. Here, the authors choose a simple and environmetally benign, meglumine catlyzed approach [24] for the preparation of titled acylhydrazones.

2. EXPERIMENTAL

2.1. Material and Methods

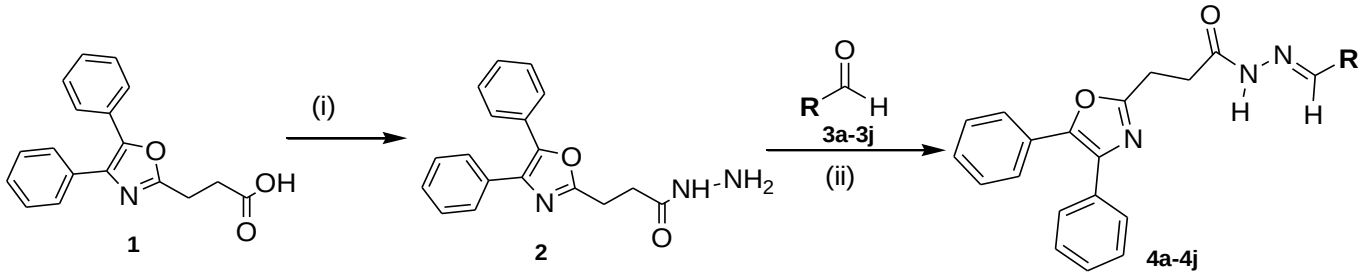
All the chemicals were purchased from Merck, Sigma-Aldrich, Finar and were used without further purification. The solvents were purchased and dried according to standard procedures prior to use. The reactions were monitored by using pre-coated Merck 60 F254 TLC silica gel plates (0.25 mm with thickness). Column chromatography was performed for purification, utilizing silica gel (60-120 mesh). A Cintex melting point apparatus was used to determine the melting points. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum one FT-IR spectrometer. A Varian 400 MHz spectrometer was utilized to record the ^{1}H NMR and ^{13}C-NMR spectra in $CDCl_3$/DMSO-d_6. Chemical shifts are presented in δ ppm, employing TMS as internal reference. A Jeol SX-102 spectrometer was used to record the Mass spectra.

2.2. Synthesis of 3-(4,5-diphenyloxazol-2-yl) propanehydrazide (2)

To a solution of 3-(4,5-diphenyl-1,3-oxazol-2-yl) propanoic acid (40 mmol) dissolved in CH_3CN (40 mL). HOBt (36 mmol) EDC (36 mmol) were added consecutively at room temperature. Then the whole mixture was stirred at room temperature, and progress of the reaction was monitored by TLC until all of the total acid was converted. Next, the resulting mixture was then slowly added to a solution of cyclohexene (1 mL) and hydrazine (60 mmol) and in CH_3CN (20 mL) followed by the addition of water (40 mL). The aqueous CH_3CN mixture was extracted with EtOAc followed by a carbonate wash of the organic layer to remove HOBt. Removal of the solvents using rotator evaporator yielded the respective hydrazide **2** as light yellow crystalline solid which is confirmed by using the data, mp: 170-172°C; IR (KBr) ν_{max}/cm^{-1} 3476, 3232, 3045, 3016, 1623, 1610, 1443, 1220, 1049; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (t, 2H), 3.17 (t, 2H), 4.62 (s, 1H, -NH), 4.65 (s, 2H, -NH_2) 7.21-7.34 (m, 6H), 7.54-7.65 (dd, 4H); Molecular formula $C_{18}H_{17}O_2N_3$; Mass *m/z*, 308.18 $[M+1]^+$.

2.3. General procedure for the preparation of titled compounds 4a-4j

To a mixture of hydrazine (1 mmol) and carbonyl compound (1 mmol), meglumine (0.15 mmol) in aqueous-ethanol (1:1, 4 ml) was added. The reaction mixture was stirred at room temperature. Progress of the reaction was monitored by TLC, using ethyl acetate and hexane (1:4). After completion of the reaction, the solution was washed with ethyl acetate (7 mL) and water (3 mL) for 5 times and then the product was extracted with ethyl acetate. The organic phase was dried over anhydrous sodium sulphate, and the solvent was evaporated using rotatory evaporator. The crude reaction mixture was purified on asilica gel (60–120 mesh) column by chromatography to obtain the final product which was characterized by NMR (^{1}H and ^{13}C), IR, and mass spectral data.



Where
3a; R = Phenyl
3b; R = *o*-methoxy phenyl
3c; R = *m*-tolyl
3d; R = *o*-nitrophenyl
3e; R = *p*-tolyl
3f; R = *m*-methoxyphenyl
3g; R = *p*-bromophenyl
3h; R = *p*-nitrophenyl
3i; R = *p*-methoxy phenyl
3j; R = *m*-nitrophenyl

4a; R = Phenyl
4b; R = *o*-methoxy phenyl
4c; R = *m*-tolyl
4d; R = *o*-nitrophenyl
4e; R = *p*-tolyl
4f; R = *m*-methoxyphenyl
4g; R = *p*-bromophenyl
4h; R = *p*-nitrophenyl
4i; R = *p*-methoxy phenyl
4j; R = *m*-nitrophenyl

Scheme 1: Synthetic protocol of N'-aryl-3-(4,5-diphenyloxazol-2-yl)-propanehydrazides

Reagents and conditions: (i) HOBt, EDC, CH_3CN, N_2H_4, Cyclohexene 90%, (ii) Meglumine, EtOH/H_2O (1:1), RT, 1h.

2.4. Antimicrobial evaluation

The *in vitro* microbial activity of prepared compounds **4a-4j** was determined by well diffusion method [25]. One day old bacterial cultures were used for antibacterial analysis. Bacterial culture plates were prepared by pour plate method, by adding about 0.3 mL of the each bacterial suspension into sterile petri plates before adding the molten state nutrient agar. After solidification, 8 mm diameter wells were made with sterile cork borer. The test samples were prepared by dissolving 2 mg in 500 µL DMSO. Wells were filled with 100 µL of the sample. The plates were incubated at 37°C for each 24h. The diameter of the zone of inhibition was measured after incubation. Triplicates were maintained for each sample and bacterial species. Standard antibiotic, Streptomycin with similar concentration was utilized as positive control. The average zone of inhibition was calculated and compared with that of standard. A similar procedure was adopted for examining the antimicrobial activity against the other organisms.

3. RESULTS AND DISCUSSION

3.1. Synthesis

The synthetic protocol used for the synthesis of *N'-aryl-3-(4,5-diphenyloxazol-2-yl)-propanehydrazides* was shown in Scheme 1. Initially, under reaction conditions 3-(4,5-diphenyl-1,3-oxazol-2-yl) propanoic acid (Oxoprozin) **1** was reacted with hydrazine hydride in CH_3CN to produce the respective 3-(4,5-diphenyloxazol-2-yl)propanehydrazide **2** in good yield. Finally, the acid hydrazide was condensed with different aryl aldehydes **3a-3j** in meglumine in aqueous-ethanol solution over one hour time period to afford the respective acylhydrazone derivatives **4a-4j** with good yields, and the results are indicated in Table 1.

3.2. Spectral characterization of the synthesized compounds 4a-4j

N'-benzylidene-3-(4,5-diphenyloxazol-2-yl)propane hydrazide (4a): mp 160-162°C; yield 78%, IR (KBr) ν_{max}/cm^{-1} 3134, 3025, 2967, 2934, 1671, 1635, 1443,

1256, 1232, 1061; ^{1}H NMR (400 MHz, $CDCl_3$) 3.17-3.32 (m, 4H), 7.16 (d, 2H, *J* =6.9), 7.29-7.40 (m, 7H), 7.59-7.68 (m, 5H), 7.76 (s, 1H), 9.21 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 27.3, 123.3, 127.1, 129.7, 130.2, 130.4, 130.8, 131.4, 131.7, 132.5, 132.8, 135.6, 138.7, 141.5, 143.7, 162.2, 167.3; Molecular Formula $C_{26}H_{23}N_3O_2$; Mass *m/z*, 396.18 $[M+1]^+$.

***N'-(2-methoxybenzylidene)-3-(4,5-diphenyloxazol-2-yl)- propanehydrazide* (4b):** mp 156-158ºC; yield 82%, IR (KBr) ν_{max}/cm^{-1} 3435, 3152, 3049, 2935, 2826, 1656, 1599, 1429, 1379, 1339, 1252, 1133, 1016; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.21-3.32 (m, 4H), 3.79 (s, 3H), 6.86 (d, 1H, *J* =7.2,), 6.92 (t, 1H, *J* =7.2), 7.23-7.32 (m, 7H), 7.49 (d, 2H, J=5.2), 7.59 (d, 2H), 7.87 (d, 1H, J =7.2), 8.15 (s, 1H), 8.71 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 30.5, 56.7, 110.5, 119.9, 122.4, 125.9, 126.3, 127.2, 128.1, 128.4, 128.7, 128.7, 128.8, 129.2, 130.9, 131.8, 138.4, 144.1, 156.8, 161.3, 172.8; Molecular Formula $C_{26}H_{23}N_3O_3$; Mass m/z, 426.21 $[M+1]^+$.

***N'-(3-methylbenzylidene)-3-(4,5-diphenyloxazol-2-yl)propanehydrazide* (4c):** mp 162-164ºC; yield 75%, IR (KBr) ν_{max}/cm^{-1} 3165, 3029, 2935, 2903, 1643, 1631, 1427, 1263, 1233, 1044; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.29-3.45 (m, 4H), 7.12 (d, 2H, *J* =6.9), 7.21-7.36 (m, 7H), 7.59-7.69 (m, 5H), 7.76 (s, 1H), 9.26 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 23.5, 30.6, 126.5, 129.2, 129.6, 130.2, 130.5, 130.8, 131.5, 131.9, 132.4, 132.8, 135.3, 139.4, 142.6, 146.3, 162.4, 170.1; Molecular Formula $C_{26}H_{23}N_3O_2$; Mass *m/z*, 410.18 $[M+1]^+$.

***N'-(2-nitrobenzylidene)-3-(4,5-diphenyloxazol-2-yl)propanehydrazide* (4d):** mp 145-147ºC; yield 70%, IR (KBr) ν_{max}/cm^{-1} 3409, 3065, 2958, 2932, 2231, 1660, 1589,1472,1438, 1216, 1166,1059; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.23-3.42 (m, 4H), 7.32-7.41 (m, 6H), 7.48 (d,1H, *J* =7.9 Hz), 7.48-7.61 (m, 5H), 8.01 (d, 1H, *J* =8.3), 8.04 (d, 1H), 8.26 (s, 1H, N=CH-), 9.17 (s, 1H, O=C-NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 33.0, 122.6, 124.6, 126.5, 126.7, 127.4, 127.9, 128.3, 128.5, 128.7, 129.0, 129.4, 130.1, 131.9, 132.7, 134.9, 137.9, 144.8, 147.6, 161.2, 172.8; Molecular Formula $C_{25}H_{20}N_4O_4$; Mass *m/z*, 441.20 $[M+1]^+$.

***N'-(4-methylbenzylidene)-3-(4,5-diphenyloxazol-2-yl)- propanehydrazide* (4e):** mp 156-158ºC; yield 75%, IR (KBr) ν_{max}/cm^{-1} 3155, 3039, 2949, 2915, 1651, 1621, 1416, 1258, 1228, 1059; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 3.19-3.35 (m, 4H), 7.21 (d, 2H, *J* =6.9), 7.33-7.45 (m, 7H), 7.61-7.74 (m, 5H), 7.81 (s, 1H), 9.39 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 22.3, 29.3, 125.3, 128.1, 128.7, 129.2, 129.4, 129.8, 130.4, 130.9, 131.4, 132.3, 134.7, 139.6, 143.5, 145.6, 161.2, 169.1; Molecular Formula $C_{26}H_{23}N_3O_2$; Mass *m/z*, 410.22 $[M+1]^+$.

***N'-(3-methoxybenzylidene)-3-(4,5-diphenyloxazol-2-yl)- propanehydrazide* (4f):** mp 176-178ºC; yield 78%, IR (KBr) ν_{max}/cm^{-1} 3507, 3187, 3016, 2935, 2856, 1643, 1638, 1521, 1432, 1276, 1168, 1047; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.24-3.38 (m, 4H), 3.74 (s, 3H), 7.21 (d, 2H), 7.31-7.49 (m, 6H), 7.57-7.68 (m, 5H), 7.78 (s, 1H), 9.51 (S, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 28.4, 52.8, 113.0, 121.3, 122.1, 125.9, 126.2, 126.9, 127.9, 128.4, 128.8, 128.8, 130.1, 131.7, 132.3, 138.4, 144.6, 158.6, 163.6, 173.8; Molecular Formula $C_{26}H_{23}N_3O_4$; Mass *m/z*, 442.21 $[M+1]^+$.

***N'-(4-bromobenzylidene)-3-(4,5-diphenyloxazol-2-yl) propanehydrazide* (4g):** mp 152-154ºC; yield 72%, IR (KBr) ν_{max}/cm^{-1} 3463, 3184, 3058, 2964, 2909, 1660, 1572, 1402, 1358, 1265, 1216, 1067; ^{1}H NMR (400 MHz, $CDCl_3$); δ 3.28-3.43 (m, 4H), 7.38-7.43 (m, 6H), 7.49 (d, 1H, *J* 8.2), 7.55-7.68 (m, 5H), 8.16(d, 1H), 8.21 (d, 1H), 8.36 (s, 1H), 9.34 (S, 1H) ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.1, 29.9, 122.9, 125.9, 126.4, 127.9, 128.0, 128.4, 128.5, 128.6, 128.7, 129.0, 129.7, 130.2, 132.5, 132.9, 135.2, 135.7, 142.3, 145.3, 162.3, 174.3; Molecular Formula $C_{25}H_{20}N_3O_2Br$; Mass *m/z*, 474.22 $[M+1]^+$.

***N'-(4-nitrobenzylidene)-3-(4,5-diphenyloxazol-2-yl)propanehydrazide* (4h):** mp 182-184ºC; yield 69%, IR (KBr) ν_{max}/cm^{-1} 3457, 3176, 3043, 2946, 2976, 2864, 1659, 1579, 1534, 1412, 1167, 1115; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.20-3.36 (m, 4H), 7.21-7.34 (m, 6H), 7.58 (dd, 4H), 7.65 (d, 2H), 7.84 (s, 1H), 8.23 (d, 2H), 9.91 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.7, 26.7, 125.9, 126.3, 126.9, 127.5, 128.3, 128.6, 128.8, 129.1, 133.3, 134.6, 139.1, 140.4, 144.9, 149.1, 163.4, 176.5; Molecular Formula $C_{25}H_{20}N_4O_4$; Mass *m/z*, 441.18 $[M+1]^+$.

***N'-(4-methoxybenzylidene)-3-(4,5-diphenyloxazol-2-yl) propanehydrazide* (4i):** mp 166-168ºC; yield 78%, IR (KBr) ν_{max}/cm^{-1} 3433, 3154, 3068, 2939, 2847, 1656, 1589, 1443, 1367, 1338, 1248, 1129, 1021; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.21-3.40 (m, 4H), 3.79 (s, 3H), 6.79 (d, 1H), 6.86 (t, 1H), 7.31-7.43(m, 7H),

7.64 (d, 2H), 7.54 (d, 2H), 7.18 (d, 1H), 7.95 (s, 1H), 8.65 (S, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 31.4, 57.3, 114.2, 123.4, 125.0, 126.6, 126.8, 127.5, 128.1, 128.6, 128.9, 129.6, 130.2, 131.7, 132.5, 139.5, 144.7, 155.0, 163.8, 171.8; Molecular Formula $C_{26}H_{23}N_3O_3$; Mass *m/z*, 426.22 $[M+1]^+$.

***N'-(3-nitrobenzylidene)-3-(4,5-diphenyloxazol-2-yl)- propanehydrazide* (4j):** mp 150-152°C; yield 72%, IR (KBr) ν_{max}/cm^{-1} 3443, 3179, 3012, 2926, 1676, 1545, 1521, 1443, 1365, 1252, 1163, 1072; ^{1}H NMR (400 MHz, $CDCl_3$); δ 3.25-3.42 (m, 4H, CH_2-CH_2), 7.23 (t, 1H, *J* 7.8, 7.6, Ph-H), 7.30-7.40 (m, 6H), 7.50 (t, 2H), 7.60 (dd, 4H), 7.76 (s, 1H), 7.75 (s, 1H), 10.09 (s, 1H);^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 31.2, 125.5, 126.8, 127.4, 128.1, 128.8, 129.3, 129.5, 129.7, 130.0, 130.2, 130.5, 130.8, 132.5, 134.2, 136.5, 138.8, 144.6, 148.1, 164.1, 174.4; Molecular Formula $C_{25}H_{20}N_4O_4$; Mass *m/z*, 441.19 $[M+1]^+$.

Table 1: Synthetic results of compounds 4a-4j

Compound	R	Yield(%)	M.P (°C)
4a	Phenyl	72	160-162
4b	*o*-methoxy phenyl	82	156-158
4c	*m*-tolyl	74	162-164
4d	*o*-nitrophenyl	70	145-147
4e	*p*-tolyl	76	156-158
4f	*m*-methoxyphenyl	79	176-178
4g	*p*-bromophenyl	70	152-154
4h	*p*-nitrophenyl	68	182-184
4i	*p*-methoxy phenyl	80	166-168
4j	*m*-nitrophenyl	71	150-152

3.3. Anti-microbial activity

The *in vitro* anti-microbial activity of synthesized *N'-aryl-3-(4,5-diphenyloxazol-2-yl)- propanehydrazide* analogs **4a-4j** was determined by well diffusion method [25]. The compounds were tested against bacterial strains *Xanthomonas campestris*, *Bacillius megaterium* (gram positive), *Escherichia coli* (gram negative) and the fungal strain *candida albicans*. The diameter of zone of inhibition, exhibited by the tested compounds for the bacterial strains at a concentration of 100uL, as per the procedure is shown in Table 2.

Table 2: Antimicrobial evaluation of novel compounds (4a-4j)

S. NO.	Compound	*Zone of inhibition in mm*			
		***XC*[a]**	***EC*[b]**	***BM*[c]**	***CA*[d]**
1	**4a**	18	12	12	11
2	**4b**	11	10	-	13
3	**4c**	10	11	09	12
4	**4d**	13	11	09	
5	**4e**	14	09	-	11
6	**4f**	20	10	09	11
7	**4g**	12	11	09	10
8	**4h**	14	11	11	12
9	**4i**	21	11	10	10
10	**4j**	11	13	13	12
Streptomycin (Standard as positive control)		27	38	36	37

XC[a] Xanthomonas campestris; EC[b] Escherichia coli; BM[c] Bacillus megaterium; CA[d] Candida albicans; "-" no zone of inhibition

The outcome of biological studies of the tested compounds **4a-4j** reveals that they possess antimicrobial activities. From the results of this screening, it has been observed that compounds **4i**, **4f** and **4a** showed superior activity against *Xanthomonas campestris* with zone of inhibition as 21, 20, 18 cm respectively, when compared with the zone of standard streptomycin as 27 cm. The compounds **4j**, **4a** exhibited moderate activity against

Escherichia coli with zone of inhibitions as 13 and 12 mm, against the standard of streptomycin as 38 mm. The compounds **4j**, **4a** and **4h** showed good activity against *Bacillus megaterium* with zone of inhibitions as 13, 12, and 11 mm respectively against the standard of streptomycin as 36 mm. While the compounds **4a-4j** are moderately active against the *Escherichia coli* and *Candida albicans* with zone of inhibition as 12 mm and 13 mm against the standard of streptomycin as 37 mm.

4. CONCLUSION

In summary, the authors have described the synthesis, *in vitro* anti microbial properties of a number of *N'-aryl-3-(4,5-diphenyloxazol-2-yl)- propanehydrazides*. Most of the compounds are active against various bacterial strains, **4a, 4b, 4i** and **4j** showed excellent inhibitory activity against different tested microbial strains. Finally, we believe that this call of hydrazone derivatives presents an interesting profile for further experimental investigations especially in the area of anti-microbial research. Further work on these scaffolds may help for invention of lead molecules in future.

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