Original Article

Synthesis and Characterization of 2-phenyl-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) - 1, 3, 4-oxadiazole Scaffolds for Assessing Their Medicinal Potentials

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ABSTRACT

Objective: The present research is aimed at the discovery and development of 1-phenyl-3-(3,4,5-trimethoxyphenyl)-1H-pyrazole derivatives as a series of novel 1, 3, 4-oxadiazoles (7a-7h) through iodine-catalyzed oxidative cyclization of the hydrazone derivatives (6a-6h) in the presence of potassium carbonate as base and DMSO as solvent in good toexcellent yields. **Methods:** The structures of all the newly synthesized compounds (6a-6h) and(7a-7h) were well characterized by IR, 1H NMR, 13C NMR and HRMS. Furthermore, allthe synthesized compounds (6a-6h and 7a-7h) were evaluated for their antimicrobial andanti-oxidant activities. **Results:** The research results revealed that the compound 6d (Z)-*2-bromo-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide)* has antimicrobial potent while the synthesized compounds 6a *(Z)-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide), 6e (Z)-2, 5-dichloro-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide), 7e (2-(2, 5-dichlorohenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole)* and 7f *(2-(3, 5-dichlorophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole)* exhibited strong antioxidant activity compared to the control BHT. **Conclusion:** The novel hydrazonessynthesized and 1, 3, 4 oxadiazole derivatives may be suggested for their establishment in chemical class of antimicrobial and antioxidant agents in new drug discovery and medicinal research.

Key words: Hydrazones, Oxadiazoles, Pyrazole, Anti-microbial, Anti-oxidant activity.

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INTRODUCTION

The synthesis and biological evaluation of 1, 3, 4-oxadiazoles containing compounds have increased considerably in the last two decades. 1,3,4-Oxadiazole is an important heterocyclic compound which contains two carbons, two nitrogen's, one oxygen atom and two double bonds in a five-membered ring with general formula $C_2H_2ON_2$. Potential pharmacological activity of 1, 3, 4-oxadiazoles is due to the presence of toxophoric -N=C-O- linkage which may react with the nucleophilic centres of the microbial cell. 1, 3, 4-Oxadiazole and its derivatives has attracted considerable attention in the medicinal, material and pesticide chemistry.[1] The various biological and pharmaceutical properties possessed by this important structural motif has attracted the researchers for the development of new drug molecules.[2] The 1, 3, 4-oxadiazole compounds are generally synthesized by the oxidative cyclization of hydrazones which were prepared by the reaction of aromatic hydrazides with aromatic aldehydes. The various reagents employed for the oxidative cyclization of 1, 3, 4-Oxadiazole includes Lead tetraacetate, Lead dioxide, Potassium Permanganate, Chloramine-T, Ferric chloride and Iodobenzenediacetate. Examples of com-

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pounds containing the 1, 3, 4-oxadiazole unit which are currently used in clinical medicine are: Raltegravir an antiretroviral drug and Zibotentan an anticancer agent, Vadrin a leprostatic drug and eudromil a hypnotic drug are a few examples.

1, 3, 4-oxadiazole derivatives have displayed a broad spectrum of biological activities such as antimicrobial[3], antioxidant[4], anticancer[5], anticonvulsant[6], antitubercular[7], antiviral[8], antimalarial[9] and analgesic and anti-inflammatory.[10] In addition to the various biological activities the 1, 3, 4-oxadiazoles are also found to possess potential agrochemical use[11] due to their wide spectrum of insecticidal[12] and acaricidal.[13] Properties attained by interfering with insect's chitin biosynthesis.[14] This class of materials also has gained the significance of modern applications such as fluorescence, scintillators and photographic materials.[14] They are of great interest as structural units in polymeric membranes designed for gas separation applications.[15] and as emitting layers in electroluminescent devices.[16] respectively.

Among the 1, 3, 4-oxadiazoles, pyrazole containing 2, 5-disubstituted-1, 3, 4-oxadiazoles are found to have considerable interest in medicinal chemistry because of their various biological characterized possessed by these compounds like antimicrobial,[17] antioxidant,[18] DNA photocleavage activity,[19] anticancer,[20] anti-inflammatory[21] and antiviral[22] activities.

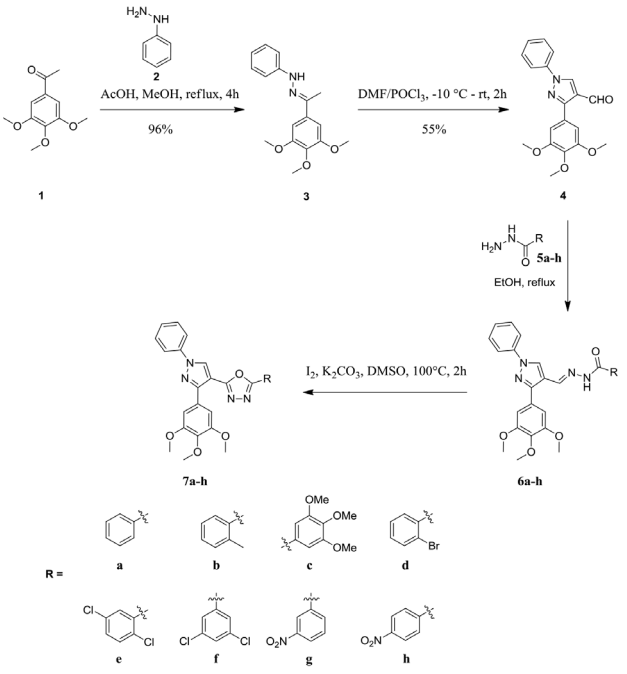
On the other hand, hydrazones are of considerable interest in synthetic chemistry and are broadly considered for studies as reaction intermediates or reactants since they can readily undergo various ring closure reactions.[23] Hydrazones are molecules containing highly reactive azomethine group (CO-NH-N=CH) and thus useful in new drug development.[24] The hydrazones can easily be synthesised by the condensation of an aldehyde or ketone with primary amine.[25] Hydrazones were also found adequate importance in organic synthesis since they served as an intermediate compounds in the synthesis of heterocyclic compounds like 1, 3, 4-oxadiazoles.[26] The hydrazone derivatives are found to posses various biological activities such as antimicrobial[27], antioxidant[28], antitubercular,[29] anti cancer,[30] antiproliferative,[31] analgesic and anti-inflammatory[32] respectively. Among the hydrazone derivatives pyrazole substituted hydrazone derivatives are known to possess various biological activities such as antibacterial,[33] antifungal,[34] anticancer,[35] antioxidant,[36] anti-inflammatory,[37] antitumor and antiangiogenesis[38] and antiplatelet activities.[39]

Pyrazole framework plays significant role in biologically active compounds and represents an interesting template for medicinal and combinatorial chemistry.[40] Compounds containing this heterocycle exhibit antimicrobial,[41] anti-oxidant,[42] anti-inflammatory,[43] antitubercular,[44] anticancer activity,[45] antiviral,[46] antidepressant and anti-convulsant activities.[47] Some arylpyrazoles were reported to have non-nucleoside HIV-1 reverse transcriptase inhibitory activity.[48] Extensive studies have been dedicated to arylpyrazole derivatives such as Celecoxib, a well-known cyclooxygenase-2 inhibitor.[49]

Based on the above-mentioned literary observations and with a view to search for new, potent, selective, and less toxic antimicrobial and anti-oxidant agents it is proposed to synthesize some novel pyrazole-linked hydrazones which were further converted into 2, 5-disubstituted 1, 3, 4-oxadiazoles.

MATERIALS AND METHODS

The chemicals employed for the present research work were commercially procured from Alfa Aesar. Melting points were determined in open glass capillaries on a Stuart SMP30 apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Shimadzu FTIR 8400S spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DPX 400 spectrophotometer using tetramethylsilane (TMS) as an internal standard, $CDCl_3$ and DMSO-*d6* as solvents and the signals are reported as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), m (multiplet) and coupling constants in Hz. HRMS spectra were recorded on a Xevo QTof mass spectrometer. Silica gel



Scheme 1: Synthesis of 2-phenyl-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazoles (7a-7h).

60 F24 of Merck pre-coated plates were employed for their thin layer chromatography (TLC) analysis to check the purity of the compounds, the spot being located under UV light and iodine vapours.

Synthesis

The title compounds were synthesized by the following steps.

Synthesis of 1-(1-(3, 4, 5-trimethoxyphenyl) ethylidene)-2-phenylhydrazine (3).[50]

To a solution of 1-(3, 4, 5-trimethoxyphenyl) ethanone **1** (5 g, 19 mmol) in methanol (40 mL) was added phenyl hydrazine **2** (2.1 g, 19 mmol) followed by glacial acetic acid (15 mL) at room temperature. The resulting reaction mixture was heated to reflux for 3 h. TLC showed completion of starting material (TLC System: 20% Ethylacetate in hexane, R_f: 0.5). The solvent was evaporated under reduced pressure, diluted with ice water (25 mL), stirred for 15 min at 10°C and filtered the precipitated solid, washed with ice water (20 mL) followed by n-pentane (20 mL) and dried under vacuum to afford 1-(1-(3, 4, 5-trimethoxyphenyl) ethylidene)-2-phenylhydrazine (**3**).

Synthesis of 3-(3, 4, 5-trimethoxypheyl)-1-phenyl-1H-pyrazole-4 carbaldehyde (4).[51]

Phosphorus oxychloride (6.2 ml, 66 mmol) was added to N, N-Dimethylformamide (26.5 ml, 339 mmol) at -5 to 0°C drop wise over a period of 10 min, stirred at the same temperature for 30 min and added compound **3** (6.6 g, 22 mmol) dissolved in DMF (10 ml) dropwise at -5°C over a period of 15 min. The reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. The completion of the reaction was monitored by TLC. After completion, the reaction mixture was slowly added to ice cold water and basified with saturated $NaHCO_3$ solution to adjust the pH 7-8, stirred for 1 h at room temperature and filtered the precipitated solid, washed with water and dried under vacuum to get the crude compound. The crude compound was washed with methanol, filtered and dried under vacuum to afford pure compound **4**.

General procedure for the synthesis of hydrazone derivatives 6a-6h.[52]

A suspension of 1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazole-4-carbaldehyde **4** (0.44 mmol) and hydrazides (**5a-5h**) (0.44 mmol) in ethanol (7 mL) was heated to reflux for 7-8 h. After completion, the precipitated solid was filtered, washed with minimum amount of ethanol and dried under vacuum to obtain hydrazone derivatives (**6a-6h**).

General procedure for the synthesis of 1, 3, 4-oxadiazole dervatives 7a-7h.[53]

To a stirred solution of compound **(6a-6h)** (0.22 mmol) in DMSO was added anhydrous K_2CO_3 (0.66 mmol) followed by Iodine (0.26 mmol) and heated to 100°C for 1 h. After completion of reaction, the reaction mixture was cooled to room temperature and treated with 5% $Na_2S_2O_3$ solution (5 ml), extracted with ethylacetate (25 ml). The organic layer was separated and washed with water and brine solution, dried over anhydrous Na_2SO_4, concentrated under reduced pressure to obtain the crude product. The crude solid product was washed with diethyl ether, filtered and dried under vacuum to afford oxadiazole derivatives (**7a-7h**).

The physicochemical and the spectral data of the synthesized compounds (6a-6h) and (7a-7h) are depicted as follows

(Z)-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide (6a). Off-white solid, M.P: 213-215°C. Yield: 75%. Chemical formula: $C_{26}H_{24}N_4O_4$. FT-IR (KBr, cm^{-1}): 1649 (C=O), 1557 (C=N), 1125 (Ar-O). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 3.71 (*3.72, s, 3H, OCH_3), 3.87 (*3.82, s, 6H, $2OCH_3$), 6.99 (*7.08, s, 2H, Ar-H), 7.36 (t, 1H, Ar-H, J = 7.2 Hz), 7.48– 7.56 (m, 5H, Ar-H), 7.87 (d, 2H, Ar-H, J = 7.6 Hz), 8.01 (d, 2H, Ar-H, J = 8.0 Hz), 8.57 (*8.67, s, 1H, CH=N), 8.97 (*9.10, s, 1H, Pyrazole-H), 11.67 (br s,1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.02, 60.06, 106.02, 116.91, 118.89, 126.96, 127.44, 127.54, 128.43, 129.57, 131.62, 133.57, 137.88, 139.03, 141.16, 151.97, 152.99, 162.77. HRMS: Calculated for $C_{26}H_{24}N_4O_4$, 456.18, found: 457.1705 $[M+H]^+$

(Z)-2-methyl-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide **(6b).** Off-white solid, M.P: 206-208°C. Yield: 71%. Chemical formula: $C_{27}H_{26}N_4O_4$. FT-IR (KBr, cm^{-1}): 1651 (C=O), 1555 (C=N), 1127 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 2.48 (s, 3H, Ar-CH_3), 3.70 (s, 3H, OCH_3), 3.86 (s, 6H, $2OCH_3$), 6.98 (s, 2H, Ar-H), 7.25-7.29 (m, 2H, Ar-H), 7.30-7.42 (m, 3H, Ar-H), 7.53 (t, 2H, Ar-H, J = 7.76 Hz), 8.02 (d, 2H, Ar-H, J = 8.0 Hz), 8.44 (s, 1H, CH=N), 8.98 (s, 1H, Pyrazole-H), 11.59 (br s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 19.24, 56.00, 60.07, 105.89, 116.84, 118.86, 125.64, 126.97, 127.36, 127.42, 127.50, 129.60, 129.83, 130.58, 135.45, 135.78, 137.86, 139.03, 140.78, 151.81, 152.99, 164.82. HRMS: Calculated for $C_{27}H_{26}N_4O_4$, 470.20, found: 471.1907 $[M+H]^+$

(Z)-3, 4, 5-trimethoxy-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide **(6c):** Off-white solid, M.P: 203-205°C. Yield: 82%. Chemical formula: $C_{29}H_{30}N_4O_7$.

FT-IR (KBr, cm^{-1}): 1636 (C=O), 1583 (C=N), 1123 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.71 (s, 6H, 2OCH_3), 3.84 (s, 6H, 2OCH_3), 3.87 (s, 6H, 2OCH_3), 7.01 (s, 2H, Ar-H), 7.18 (s, 2H, Ar-H), 7.38 (t, 1H, Ar-H, J = 7.2 Hz), 7.53 (t, 2H, Ar-H, J = 7.68 Hz), 8.02 (d, 2H, Ar-H, J = 8.08 Hz), 8.55 (s, 1H, CH=N), 8.99 (s, 1H, Pyrazole-H), 11.53 (br s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.05, 56.13, 60.08, 60.13, 105.25, 106.10, 116.89, 118.91, 126.99, 127.46, 127.53, 128.79, 129.59, 137.94, 139.03, 140.39, 141.14, 151.95, 152.69, 153.01, 162.37. HRMS: Calculated for $C_{29}H_{30}N_4O_7$, 546.21, found: 547.1993 $[M+H]^+$

***(Z)-2-bromo-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide* (6d).** Off-white solid, M.P: 177-179°C. Yield: 70%. Chemical formula: $C_{26}H_{23}BrN_4O_4$. FT-IR (KBr, cm^{-1}): 1648 (C=O), 1551 (C=N), 1127 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.70 (*3.72, s, 3H, OCH_3), 3.86 (*3.84, s, 6H, 2OCH_3), 6.99 (*6.83, s, 2H, Ar-H), 7.35-7.41 (m, 2H, Ar-H), 7.42-7.56 (m, 4H, Ar-H), 7.72 (*7.63, d, 1H, Ar-H, J = 7.84), 8.02 (*7.83, d, 2H, Ar-H, J = 8.08), 8.41(*8.30, s, 1H, CH=N), 9.0 (s, 1H, Pyrazole-H), 11.72 (*11.81, br s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.01, 60.07, 105.65, 105.89, 116.53, 116.61, 118.87, 119.07, 119.46, 126.26, 127.00, 127.18, 127.35, 127.74, 129.04, 129.26, 129.59, 130.61, 131.46, 132.16, 132.83, 137.47, 137.64, 137.88, 138.89, 139.00, 141.45, 151.72, 151.87, 152.99, 162.91, 168.66. HRMS: Calculated for $C_{26}H_{23}BrN_4O_4$, 534.09, found: 535.0853 $[M+H]^+$

***(Z)-2, 5-dichloro-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide* (6e).** Off-white solid, M.P: 179-181°C. Yield: 76%. Chemical formula: $C_{26}H_{22}Cl_2N_4O_4$. FT-IR (KBr, cm^{-1}): 1654 (C=O), 1561 (C=N), 1127 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.70 (*3.71, s, 3H, OCH_3), 3.86 (*3.83, s, 6H, 2OCH_3), 6.99 (*6.81, s, 2H, Ar-H), 7.35-7.39 (m, 1H, Ar-H), 7.50-7.59 (m, 4H, Ar-H), 7.71 (s, 1H, Ar-H), 8.02 (*7.86, d, 2H, Ar-H, J = 7.92 Hz), 8.40 (*8.23, s, 1H, CH=N), 9.01 (s, 1H, Pyrazole-H), 11.80 (*11.93, br s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.02, 60.06, 105.66, 105.94, 116.47, 118.89, 119.09, 126.58, 127.03, 127.30, 127.83, 128.42, 128.66, 128.95, 129.31, 129.59, 130.34, 130.79, 131.14, 131.53, 131.87, 136.75, 137.90, 138.45, 138.97, 141.94, 151.77, 151.96, 152.98, 160.57, 166.51. HRMS: Calculated for $C_{26}H_{22}Cl_2N_4O_4$, 524.10, found: 525.0982 $[M+H]^+$

***(Z)-3, 5-dichloro-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide* (6f)**. Off-white solid, M.P: 224-226°C. Yield: 84%. Chemical formula: $C_{26}H_{22}Cl_2N_4O_4$. FT-IR (KBr, cm^{-1}): 1686 (C=O), 1555 (C=N), 1120 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.72 (s, 3H, OCH_3), 3.88 (s, 6H, 2OCH_3), 6.99 (s, 2H, Ar-H), 7.38 (t, 1H, Ar-H, J = 7.4 Hz), 7.54 (t, 2H, Ar-H, J = 7.76 Hz), 7.86-7.91 (m, 3H, Ar-H), 8.02 (d, 2H, Ar-H, J = 7.96 Hz), 8.54 (s, 1H, CH=N), 9.01 (s, 1H, Pyrazole-H), 11.80 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.06, 60.07, 106.10, 116.64, 118.94, 126.34, 127.04, 127.35, 127.65, 129.58, 131.01, 134.39, 136.78, 137.96, 138.99, 142.24, 152.16, 153.00, 159.97. HRMS: Calculated for $C_{26}H_{22}Cl_2N_4O_4$, 524.10, found: 525.1005 $[M+H]^+$

***(Z)-3-nitro-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide* (6g):** Pale yellow solid, M.P: 224-226°C. Yield: 76%. Chemical formula: $C_{26}H_{23}N_5O_6$. FT-IR (KBr, cm^{-1}): 1689 (C=O), 1559 (CH=N), 1125 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.72 (s, 3H, OCH_3), 3.88 (s, 6H, 2OCH_3), 7.01(s, 2H, Ar-H), 7.37 (t, 1H, Ar-H, J = 7.24 Hz), 7.54 (t, 2H, Ar-H, J = 7.8 Hz), 7.83 (t, 1H, Ar-H, J = 7.96 Hz), 8.03 (d, 2H, Ar-H, J = 8.0 Hz), 8.34 (d, 1H, Ar-H, J = 7.92 Hz), 8.43 (d, 1H, Ar-H, J = 8.16 Hz), 8.59 (s, 1H, CH=N), 8.72 (s, 1H, Ar-H), 9.02 (s, 1H, Pyrazole-H), 11.96 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.06, 60.07, 106.13, 116.68, 118.94, 122.23, 126.24, 127.03, 127.37, 127.66, 129.58, 130.29, 134.01, 134.92, 137.96, 138.99, 142.26, 147.79, 152.16, 153.01, 160.58. HRMS: Calculated for $C_{26}H_{23}N_5O_6$, 501.16, found: 502.1605 $[M+H]^+$

***(Z)-4-nitro-N'-((1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl) methylene) benzohydrazide* (6h).** Pale yellow solid, M.P: 243-245°C. Yield: 74%. Chemical formula: $C_{26}H_{23}N_5O_6$. FT-IR (KBr, cm^{-1}): 1681 (C=O), 1593 (CH=N), 1120 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.73 (s, 3H, OCH_3), 3.89 (*3.84, s, 6H, 2OCH_3), 7.01 (* 6.88, s, 2H, Ar-H), 7.39 (t, 1H, Ar-H, J = 7.2 Hz), 7.55 (t, 2H, Ar-H, J = 7.6 Hz), 8.04 (*7.93, d, 3H, Ar-H, J = 8.0 Hz), 8.14 (*8.29, d, 2H, Ar-H, J = 8.8 Hz), 8.37 (d, 2H, Ar-H, J = 8.8 Hz), 8.60 (*8.70, s, 1H, CH=N), 9.03 (s, 1H, Pyrazole-H), 11.96 (br s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.07, 60.09, 106.11, 116.68, 118.96, 123.65, 127.06, 127.37, 127.69, 129.10, 129.60, 137.97, 139.01, 139.24, 142.39, 149.22, 152.17, 153.02, 161.09. HRMS: Calculated for $C_{26}H_{23}N_5O_6$, 501.16, found: 502.1582 $[M+H]^+$

***2-phenyl-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole* (7a):** Off- white solid, M.P: 199-201°C. Yield: 73%. Chemical formula: $C_{26}H_{22}N_4O_4$. FT-IR (KBr, cm^{-1}): 1588 (C=N), 1124 (Ar-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.92 (s, 6H, 2OCH_3), 3.93 (s, 3H, OCH_3), 7.32 (s, 2H, Ar-H), 7.38-

7.41 (m, 1H, Ar-H), 7.47-7.55 (m, 5H, Ar-H), 7.83-7.85 (m, 2H, Ar-H), 7.99-8.01 (m, 2H, Ar-H), 8.66 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 55.99, 60.12, 105.83, 106.38, 119.02, 123.27, 126.45, 126.78, 127.48, 129.37, 129.68, 131.46, 131.99, 138.24, 138.66, 150.38, 152.64, 159.60, 163.09. HRMS: Calculated for $C_{26}H_{22}N_4O_4$, 454.16, found: 455.1639 $[M+H]^+$

***2-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-5-(o-tolyl)-1, 3, 4-oxadiazole* (7b):** Off-white solid, M.P: 204-206°C. Yield: 90%. Chemical formula: $C_{27}H_{24}N_4O_4$. FT-IR (KBr, cm^{-1}): 1584 (C=N), 1120 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 2.61(s, 3H, Ar-CH_3), 3.73 (s, 3H, OCH_3), 3.81 (s, 6H, $2OCH_3$), 7.35-7.46 (m, 5H, Ar-H), 7.48-7.52 (m, 1H, Ar-H), 7.59 (t, 2H, Ar-H, J = 7.72 Hz), 7.94 (d, 1H, Ar-H, J =7.72 Hz), 8.05 (d, 2H, Ar-H, J =7.92 Hz), 9.43 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 21.47, 56.01, 60.12, 105.89, 106.48, 119.09, 122.37, 126.33, 126.87, 127.48, 128.71, 129.68, 131.30, 131.43, 131.75, 137.67, 138.24, 138.69, 150.55, 152.65, 159.11, 163.42. HRMS: Calculated for $C_{27}H_{24}N_4O_4$, 468.18, found: 469.1665 $[M+H]^+$

***2-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-5-(3, 4, 5-trimethoxyphenyl)-1, 3, 4-oxadiazole* (7c):** Off-white solid, M.P: 177-179°C. Yield: 83%. Chemical formula: $C_{29}H_{28}N_4O_7$. FT-IR (KBr, cm^{-1}): 1588 (C=N), 1122 (Ar-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.91 (s, 18H, $6OCH_3$), 7.18 (s, 2H, Ar-H), 7.24 (d, 2H, Ar-H, J = 12.36 Hz), 7.40 (t, 1H, Ar-H, J = 7.2 Hz), 7.54 (t, 2H, Ar-H, J = 7.64 Hz), 7.85 (d, 2H, Ar-H, J = 7.96 Hz), 8.69 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 55.98, 56.09, 60.09, 60.24, 103.84, 105.86, 106.40, 118.42, 119.11, 126.87, 127.50, 129.68, 131.24, 138.17, 138.66, 140.58, 150.46, 152.59, 153.47, 159.49, 162.95. HRMS: Calculated for $C_{29}H_{28}N_4O_7$, 544.20, found: 545.1902 $[M+H]^+$

***2-(2-bromophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole* (7d):** Off-white solid, M.P: 209-211°C. Yield: 73%. Chemical formula: $C_{26}H_{21}BrN_4O_4$. FT-IR (KBr, cm^{-1}): 1586 (C=N), 1123 (Ar-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.91 (s, 3H, OCH_3), 3.93 (s, 6H, $2OCH_3$), 7.35-7.49 (m, 5H, Ar-H), 7.54 (t, 2H, Ar-H, J = 7.6 Hz), 7.75 (d, 1H, Ar-H, J = 7.92 Hz), 7.84 (d, 2H, Ar-H, J = 7.76 Hz), 7.92-7.94 (dd, 1H, Ar-H, J = 1.52, 7.68 Hz), 8.64 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.00, 60.11, 105.56, 106.45, 119.15, 119.29, 120.85, 124.52, 126.69, 127.54, 128.17, 128.51, 129.68, 131.48, 131.61, 133.28, 134.39, 138.26, 138.64, 150.59, 152.66, 159.93, 162.03. HRMS: Calculated for $C_{26}H_{21}BrN_4O_4$, 532.07, found: 533.0682 $[M+H]^+$

***2-(2,5 dichlorophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole* (7e):** Off-white solid, M.P: 219-221°C. Yield: 79%. Chemical formula: $C_{26}H_{20}Cl_2N_4O_4$. FT-IR (KBr, cm^{-1}): 1586 (C=N), 1120 (Ar-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm): 3.92 (s, 3H, OCH_3), 3.93 (s, 6H, $2OCH_3$), 7.32 (s, 2H, Ar-H), 7.39-7.44 (m, 2H, Ar-H), 7.48 (d, 1H, Ar-H, J = 8.6 Hz), 7.54 (t, 2H, Ar-H, J = 7.6 Hz), 7.84 (d, 2H, Ar-H, J = 7.72 Hz), 8.01 (d, 1H, Ar-H, J = 2.4 Hz), 8.65 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.01, 60.10, 105.49, 106.50, 119.17, 123.88, 126.71, 127.58, 129.69, 130.21, 130.55, 131.65, 132.29, 132.69, 133.03, 138.27, 138.63, 150.66, 152.65, 160.02, 160.17. HRMS: Calculated for $C_{26}H_{20}Cl_2N_4O_4$, 522.09, found: 523.0849 $[M+H]^+$

***2-(3, 5-dichlorophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole* (7f):** Off-white solid, M.P: 181-183°C. Yield: 81%. Chemical formula: $C_{26}H_{20}Cl_2N_4O_4$. FT-IR (KBr, cm^{-1}): 1589 (C=N), 1129 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.74 (s, 3H, OCH_3), 3.84 (s, 6H, $2OCH_3$), 7.42-7.45 (m, 3H, Ar-H), 7.60 (t, 2H, Ar-H, J = 7.72 Hz), 7.92 (t, 1H, Ar-H, J = 1.8 Hz), 8.02-8.05 (m, 4H, Ar-H), 9.52 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.01, 60.13, 105.58, 106.46, 119.05, 124.88, 126.49, 126.68, 127.58, 129.71, 131.24, 131.83, 135.24, 138.29, 138.59, 150.43, 152.64, 160.26, 160.91. HRMS: Calculated for $C_{26}H_{20}Cl_2N_4O_4$, 522.09, found: 523.0869 $[M+H]^+$

2-(3-nitrophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole (7g): Pale yellow solid, M.P: 176-178°C. Yield: 77%. Chemical formula: $C_{26}H_{21}N_5O_6$. FT-IR (KBr, cm^{-1}): 1590 (C=N), 1514 (Ar-NO_2), 1126 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.75 (s, 3H, OCH_3), 3.83 (s, 6H, $2OCH_3$), 7.42-7.45 (m, 3H, Ar-H), 7.60 (t, 2H, Ar-H, J = 7.64 Hz), 7.92 (t, 1H, Ar-H, J = 8.04 Hz), 8.05 (d, 2H, Ar-H, J = 7.84 Hz), 8.47 (d, 2H, Ar-H, J = 7.92 Hz), 8.71 (s, 1H, Ar-H), 9.53 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 55.99, 60.10, 105.54, 106.40, 119.08, 120.85, 124.83, 126.32, 126.68, 127.55, 129.69, 131.28, 131.76, 132.45, 138.29, 138.61, 148.28, 150.46, 152.65, 160.26, 161.59. HRMS: Calculated for $C_{26}H_{21}N_5O_6$, 499.15, found: 500.1482 $[M+H]^+$

***2-(4-nitrophenyl)-5-(1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1H-pyrazol-4-yl)-1, 3, 4-oxadiazole* (7h):** Pale yellow solid, M.P: 219-221°C. Yield: 70%. Chemical formula: $C_{26}H_{21}N_5O_6$. FT-IR (KBr, cm^{-1}): 1594 (C=N), 1517 (Ar-NO_2), 1120 (Ar-O). ^{1}H NMR (400 MHz, DMSO- d_6, δ ppm): 3.76 (s, 3H, OCH_3), 3.84 (s, 6H, $2OCH_3$), 7.44-7.47 (m, 3H, Ar-H), 7.61 (t, 2H, Ar-H, J = 8.0 Hz), 8.06 (d, 2H, Ar-H, J = 8.0 Hz),

8.30 (d, 2H, Ar-H, J = 8.8 Hz), 8.46 (d, 2H, Ar-H, J = 8.8 Hz), 9.52 (s, 1H, Pyrazole-H). ^{13}C NMR (100 MHz, DMSO-*d6*, δ ppm): 56.07, 60.17, 105.58, 106.44, 119.09, 124.65, 126.66, 127.63, 127.77, 128.91, 129.77, 131.89, 138.35, 138.64, 149.21, 150.52, 152.69, 160.57, 161.83. HRMS: Calculated for $C_{26}H_{21}N_5O_6$, 499.15, found: 500.1472 $[M+H]^+$

ANTIMICROBIAL EVALUATION[54]

Antibacterial Activity Test Microorganisms and Growth Media *Staphylococcus aureus* (MTCC 3160), *Bacillus cereus* (MTCC 1305), *E.Coli* (MTCC 443) and *Pseudomonas aeruginosa* (MTCC 2453) and *Candida albicans* were selected based on their clinical and pharmacological importance. The bacterial strains obtained from Department of Microbiology, Osmania University, were employed for evaluating antibacterial activity. The bacterial stock cultures were incubated for 24 h at 37°C on nutrient agar. The bacteria were grown on Mueller-Hinton agar plates at 37°C. The stock culture was maintained at 4°C. for the growth of fungi potato dextrose agar was used. Whatman No.1 filter paper discs of 5mm diameter were autoclaved by keeping in a clean and dry Petri plate. The discs were soaked in compound solutions for 5 h were taken as test material. After 5 h the discs were shade dried. The concentrations of compound solutions per disc are accounted for 0.1 g/1ml. Subsequently, they were carefully transferred to spread on cultured Petri plates. Filter paper discs immersed in ethanol, hexane, benzene and distilled water are prepared and used as control. To test the antibacterial activity, LB agar medium was prepared and the medium was sterilized at 121°C for 30 mins. The agar plates were prepared by pouring about 10ml of the medium into 10cm petri dishes under aseptic condition and left undisturbed for 2 h to solidify the medium. 1ml of inocculum (containing suspension) of *Staphylococcus aureus*, *Bacillus subtilis*, *E.Coli* and was poured on to the plates separately containing solidified agar media. The prepared sterile filter paper discs were impregnated with the compound solutions and shaken thoroughly and these test plates incubated for a period of 48 hrs in BOD at 37ºC for the development of inhibitory zones and the average of 2 independent readings for each organism in different compound solutions were recorded. The inhibition zones were measured after 1 day at 37ºC for bacteria. The diameter of the inhibition zone was measured and recorded with the aid of plastic ruler. Five paper discs placed in one Petri plate.

ANTIOXIDANT EVALUATION[55]

The DPPH radical-scavenging activity was determined by using the method proposed by Yen and Chen (1995). DPPH (100 lM) was dissolved in pure ethanol (96%). The radical stock solution was prepared fresh daily. The DPPH solution (1 ml) was added to 1 ml of polyphenol extracts with 3 ml of ethanol. The mixture was shaken vigorously and allowed to stand at room temperature in the dark for 10 min. The decrease in absorbance of the resulting solution was monitored at 517 nm at 10 min. The results were corrected for dilution and expressed in lM Trolox per 100 g dry weight (dw). All determinations were performed in triplicate. 2, 6-bis (1, 1-dimethylethyl)-4-methylphenol (BHT) antioxidant agents was used as positive control.

RESULTS AND DISCUSSION

Chemistry

The route for the synthesis of 2, 5-substituted 1, 3, 4-oxadiazole derivatives (7a-h) is depicted in **Scheme 1** which involves four steps. Initially, the starting material 3,4,5-trimethoxy acetophenone **1** was treated with phenyl hydrazine **2** using acetic acid and methanol as a solvent at reflux temperature to obtain the acetophenone phenylhydrazone derivative **3** in 96% yield. In the second step the acetophenone phenylhydrazone derivative **3** was treated with Vilsmeier–Haack reagent (DMF-$POCl_3$) to obtain 1-phenyl-3-(3, 4, 5-trimethoxyphenyl)-1*H*-pyrazole carboxaldehyde **4** in 50% yield. The obtained pyrazole carboxaldehyde intermediate **4** was treated with different aryl hydrazides (**5a-h**) in the presence of ethanol at reflux temperature to obtain the corresponding hydrazone derivatives (**6a-h**) which underwent iodine catalysed cyclisation using potassium carbonate as base and DMSO as solvent to afford the title compounds (**7a-h**) in 70-90% yield. All the compounds synthesized were well characterized by IR, ^{1}H NMR, ^{13}C NMR and HRMS spectral analysis. It is considerable to note that hydrazones derivatives were found to be present as a mixture of two rotameric forms in solution.[56] e.g. antiperiplanar (*ap*) and synperiplanar (*sp*) as indicated by their ^{1}H NMR spectra. The ^{1}H NMR spectra of the hydrazone compounds **6a, 6d, 6e** and **6h** revealed the duplication of some signals indicating the presence of rotamers.

Antimicrobial activity

The title compounds (**6a-h**) and (**7a-h**) were evaluated for their antimicrobial activity using *Escherichia Coli* (MTCC 443) and *Pseudomonas aeruginosa* (MTCC 2453) as g negative bacterial strains and *Staphylococcus aureus* (MTCC 3160), *Bacillus cereus* (MTCC 1305) as g posi-

Table 1: Antimicrobial activity (zone of inhibition in mm) of compounds 6a–h at various concentrations (200, 300 and 500 µg/mL).

Compound	Antibacterial activity (conc., µg/mL)												Antifungal activity		
	G negative bacteria						G positive bacteria						*C.albicans*		
	E.coli (MTCC 443)			*P. aeruginosa* (MTCC 2453)			*S.aureus* (MTCC 3160)			*B. cereus* (MTCC 1305)					
	200	300	500	200	300	500	200	300	500	200	300	500	200	300	500
6a	6	8	10	4	5	8	1	2	3	3	5	7	3	5	7
6b	4	6	8	-	-	-	8	9	12	3	5	7	-	-	-
6c	-	-	-	5	7	9	-	-	-	-	-	-	-	-	-
6d	-	-	-	-	-	-	9	11	12	-	-	-	6	7	8
6e	-	-	-	-	-	-	6	7	8	1	2	3	5	6	7
6f	4	6	8	3	4	5	8	8	12	2	4	5	-	-	-
6g	-	-	-	5	7	8	-	-	-	-	-	-	-	-	-
6h	-	-	-	5	8	9	-	-	-	-	-	-	1	2	3
Streptomycin	8	9	11	7	9	10	9	10	13	7	8	9	9	9	10

Table 2: Antimicrobial activity (zone of inhibition in mm) of compounds 7a–h at various concentrations (200, 300 and 500 µg/mL).

Compound	Antibacterial activity												Antifungal activity		
	G negative bacteria						G positive bacteria						*C.albicans*		
	E.coli (MTCC 443)			*P. aeruginosa* (MTCC 2453)			*S.aureus* (MTCC 3160)			*B. cereus* (MTCC 1305)					
	200	300	500	200	300	500	200	300	500	200	300	500	200	300	500
7a	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7c	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7d	-	-	-	2	3	4	-	-	-	-	-	-	-	-	-
7e	3	4	5	-	-	-	3	4	5	1	2	3	3	4	6
7f	-	-	-	-	-	-	-	-	-	2	3	4	-	-	-
7g	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7h	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Streptomycin	7	8	10	8	9	10	9	10	11	8	8	9	9	9	10

tive bacterial strains at different concentration levels of 200, 300 and 500 µg with Streptomycin as standard drug. The related antibacterial activities of the hydrazone derivatives are present in Table 1. The compounds **6b, 6d** and **6f** are found to have high activity at all concentrations over g positive *staphylococcus aureus*. Compound **6a** exhibited considerable activity over g negative bacterial strain *E.Coli* at all concentrations. Compounds **6c** and **6h** have responded with activity over g negative *P. aeruginosa* at 300 and 500 µg concentrations compared to the standard drug. The antifungal activity studies revealed that compound **6d** has potential activity while compounds **6a** and **6e** have moderate activities and compound **6h** showed weak activity against the fungi *C.albicans*. When compared to the standard (BHT).

The *in vitro* antibacterial studies of the oxadiazoles **7a-h** (Table 2) revealed that compound **7e** is moderate in activity while the remaining compounds did not announce any activity. The antifungal activity of the compounds **7a-h** revealed that compound **7e** exhibited good activity over the fungal species *C.albicans* at 500 µg concentration while all the other remaining compounds are inert in activity. Based on the analytical results, it is evident that compound **6d** (2-bromo substituted pyrazole hydrazone derivative) is a potential agent with significant antimicrobial activity.

Anti-oxidant activity

The antioxidant activity of the hydrazone and oxadiazole derivatives was evaluated using DPPH radical

Table 3: Antioxidant activity of compounds 6a-h by DPPH method.

Compound	Scavenging activity (IC_{50}, µM)					
	25 µM	50 µM	75 µM	100 µM	125 µM	250 µM
6a	11.9 ± 1.53	25.7 ± 1.23	36.1 ± 1.32	38.5 ± 1.42	39.4 ± 1.18	69.7 ± 1.12
6b	15.4 ± 1.30	27.7 ± 1.24	38.6 ± 1.23	39.3 ± 1.36	39.5 ± 1.32	69.8 ± 1.43
6c	-	-	-	-	-	-
6d	-	-	-	-	37.34 ± 1.54	68.26 ± 1.32
6e	12.2 ± 1.03	22.9 ± 1.22	34.3 ± 1.47	35.2 ± 1.39	35.5 ± 1.35	66.9 ± 1.54
6f	13.9 ± 1.10	25.8 ± 1.15	36.4 ± 1.30	36.9 ± 1.43	37.4 ± 1.34	68.3 ± 1.36
6g	-	-	-	-	-	-
6h	-	-	-	-	-	-
Control (BHT)	18.40 ± 0.55	28.28 ± 1.20	42.32± 1.24	45.35 ± 1.32	47.28 ± 1.44	76.38 ± 1.32

Table 4: Antioxidant activity of compounds 7a-h by DPPH method

Compound	Scavenging activity (IC_{50}, µM)					
	25 µM	50 µM	75 µM	100 µM	125 µM	250 µM
7a	-	-	-	-	-	-
7b	-	-	-	-	-	-
7c	-	-	-	-	-	-
7d	-	-	-	-	35.5 ± 1.25	66.9 ± 1.48
7e	13.9 ± 1.45	25.4 ± 1.34	36.5 ± 1.25	38.1 ± 1.37	39.2 ± 1.28	69.9 ± 1.32
7f	15.4 ± 1.12	25.8 ± 1.32	36.6 ± 1.44	38.8 ± 1.33	39.7 ± 1.47	69.8 ± 1.29
7g	-	-	-	-	-	-
7h	-	-	-	-	-	-
Control (BHT)	18.40 ± 0.55	28.28 ± 1.20	42.32 ± 1.24	45.35 ± 1.32	47.28 ± 1.44	76.38 ± 1.32

scavenging method using 2, 6-bis (1, 1-dimethylethyl)-4-methylphenol (BHT) as standard.

The DPPH radical scavenging activity results of the hydrazone derivatives (**6a-h**) at different concentrations are depicted in Table 3. The activity studies revealed that the compounds **6a**, **6b**, **6e** and **6f** exhibited strong anti-oxidant activities in all concentrations when compared to the standard BHT. Among the active compounds, compounds **6a (**the phenyl substituted derivative) and compound **6e (**the 2, 5-dichloro substituted derivative) showed excellent activities, compound **6a** being the most potent compound. Next to **6a** and **6e**, compounds **6b** and **6f** exhibited promising activities while compound **6d** showed good activity at 125**µM and 250µM** concentrations. The order of radical scavenging activities of these compounds is in the order **6a>6e>6f>6b>6d**. All the remaining compounds announced non antioxidant activity.

The DPPH radical scavenging activity results of the oxadiazole derivatives (**7a-h**) at different concentrations are depicted in Table 4. From the Table, it is evident that the compounds **7e** (2, 5-dichloro) and **7f** (3, 5-dichloro) exhibited excellent anti oxidant activities, compound **7e** being the most potent compound when compared to the standard BHT. Compound **7d** showed good activity at 125µM and 250µM concentrations while the remaining compounds announced non- antioxidant activity.

CONCLUSION

Screening of compounds **6a-h** and **7a-h** invitro for their anti-microbial activity against Streptomycin as control drug indicated that the compound **6d** (2-bromo sub-stituted pyrazole hydrazone derivative) is antimicrobial potent. The antioxidant evaluation of the same series of compounds using DPPH radical scavenging method revealed that compounds **6a**, **6e, 7e and 7f** announced strong activities when compared to the control BHT.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS USED

TLC: Thin layer chromatography; **FT-IR**: Fourier transform infrared spectroscopy; **NMR**: Nuclear magnetic resonance spectroscopy; **DMSO-**d_6: Deuterated dimethyl sulphoxide; **HRMS**: High resolution mass spectrometry; **M.P:** Melting Point; **DPPH:** 2, 2-diphenyl-1-picrylhydrazyl; **BHT:** 2, 6-bis (1, 1-dimethylethyl)-4-methylphenol; **BOD:** Bio Chemical Oxygen Demand.

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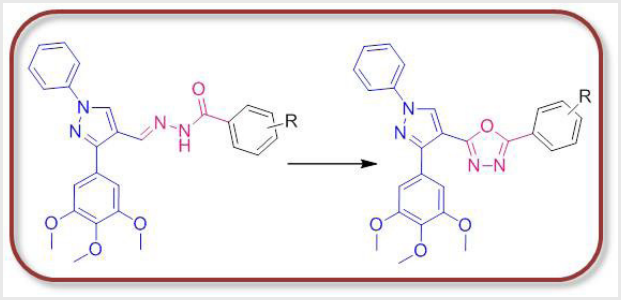
PICTORIAL ABSTRACT



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SUMMARY

- A novel 1, 3, 4-oxadiazole substituted pyrazole scaffolds **7a-h** were synthesized by the iodine catalyzed oxidative cyclization of different hydrazone derivatives **6a-h** in good to excellent yields. The hydrazone derivatives **6a-h** were obtained by heating the corresponding aldehyde intermediate **4** in ethanol with various substituted aryl hydrazides. All the final compounds were characterized by IR, NMR and HRMS spectral analysis. The *invitro* antimicrobial activity of the synthesized compounds **6a-h** and **7a-h** were screened over two g negative bacterial strains *E.Coli*, *P. aeruginosa* and two g positive bacterial strains *S. aureus*, *B. cereus* with three different concentrations of 200, 300 and 500 μg/mL using Streptomycin as standard drug. The study results revealed that the compounds **6a**, **6b**, **6d** and **6f** are with moderate to good antimicrobial activity. The compounds **6a**, **6d** and **6e** are found to have moderate to good antifungal activity. Finally the research study results revealed that the compound **6d** (2-bromo substituted pyrazole hydrazone derivative) as a potential antimicrobial agent. Furthermore, the antioxidant activity studies revealed that the compounds **6a, 6e** and **7e, 7f** exhibited potent anti oxidant activities when compared to the control drug BHT.

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