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THE SYNTHESIS OF QUINAZOLON-1,3,4-OXADIAZOLE ANALOGUES AND STUDIES OF THEIR ANTIMICROBIAL AND ANTIOXIDANT ACTIVITY

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Keywords:

1,3,4-oxadiazole, Quinazolone, Antimicrobial, Antioxidant

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ABSTRACT: A series of conjugation of two heterocycles 1, 3, 4-oxadiazole and quinazolone were synthesized and screened for antimicrobial as well as antioxidant activity. Compound4-(4-oxo-2-phenyl-quinazoline-3(4H)-yl)-benzohydrazide 3 on cyclization with different aromatic acids in the presence of phosphoryl chloride ($POCl_3$) give different 1, 3, 4-oxadiazole derivatives. Similarly, compound 3 on reaction with carbon disulphide (CS_2) gives substituted oxadiazole thione which on reaction with different halides in the presence of dimethylformamide (DMF) give oxadiazole thiones analogs 6a-6c. Structural assignments of these compounds have been made by elemental analysis, UV, IR, ^{1}H NMR, and mass spectral data. Synthesized analogs were screened for *in-vitro* growth inhibition activity against different strains of bacteria and fungi and compared with standard drugs ciprofloxacin and fluconazole. Compounds 4e and 4f have good activity against bacteria. All compounds have moderate activity against fungi. These compounds were screened for antioxidant activity by using radical scavenging DPPH assay by using ascorbic acid as a standard drug. Compounds 4e, 6a to 6c have good antioxidant activity.

INTRODUCTION: Antimicrobial agents are the most significant weapons to fight against bacterial and fungal infection. But many commonly used antibiotics are becoming less effective against infections due to the emergence of microbial resistance. In case of infection, there is an occurrence of increasing fungal infection from day to day. These fungal infections continue to grow rapidly. Present antifungal agents do not satisfy the medical need, as well as some drugs like polyene antibiotics, are most toxic.

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So, antimicrobial agents are of interest for most researchers. Heterocyclic compounds like 1, 3, 4-oxadiazole and quinazoline nucleus possess a diversity of biological activity. 1, 3, 4-oxadiazole chemistry with a broad spectrum of medicinal value has got much significance in recent years.

The activities associated with oxadiazole nucleus are antimicrobial [1-6], hepatoprotectives [7], anti-mitotic [8], anticancer [1, 9, 10], anti-inflammatory [11], anticonvulsant [12, 13], analgesic [11, 14], anti TB [15, 16], diuretic [17], antihypertensive [18] and antidepressant [19]. Quinazoline nucleus also possesses a variety of activities such as antimicrobial [20, 21], anticancer [20, 22], antiviral [22], antidiabetes [23], anticonvulsant [24], antituberculosis [25], anti-inflammatory [26] analgesics [26, *etc*. Free radicals are generated in the human body which can damage proteins, lipids, DNA, and leads to carcinogenesis, toxicity and inflammation.

Antioxidant agents prevent oxidation of a biological substrate, lower oxidative stress, decrease DNA mutation and thus block loss of cell function. Given these findings, our interest increased to undertake the synthesis and biological evolution of substituted quinazoline-1,3,4-oxadiazole analogs hoping that these compounds might show certain antimicrobial and antioxidant activity.

The composition of all compounds was obtained by elemental analysis. IR, NMR and mass spectroscopy deduced structures. The entire newly synthesized compounds were screened for antimicrobial activity by cup plate method and antioxidant by diphenylpicrylhydrazide (DPPH) radical scavenging method.

MATERIAL AND METHODS: Melting points of compounds were determined using micro-controller based Melting point apparatus, CL 725/726 and were found uncorrected. The purity of compounds was checked by thin layer chromatography using silica gel G, F_{254} precoated silica gel G (3 × 8 cm) as a stationary phase and various combinations of solvents as a mobile phase. These plates procured from E-merc, Darmstd. Theses resolved spots were visualized as brown colored spots by using iodine chamber. The IR spectra of synthesized compounds were recorded using KBr pellets in range of 4000-400 cm^{-1} on Fourier transformer IR spectrometer (Shimadzu 8700). 1H NMR (400 MHz) spectra were recorded in chloroform-d and DMSO-d6 in Amx-400 MHz liquid state NMR spectrometer BRUKER. Chemical shifts (δ) are reported in parts per million with standard internal Tetramethylsilane (TMS) as well as mass spectra (JEOL GC mate Mass Spectrometer).

The chemicals and reagents used in the present project were of AR grade and LR grade, purchased from S.D. Fine Chem. Ltd., Merck, LOBA Chemicals, Mumbai, India. Required dry pyridine and dry ethanol are prepared as per procedure are given in the book, Practical of Organic Chemistry by Vogel. Pyridine is distilled using KOH, and dry ethanol is prepared using CaO_2.

The Experimental Work Comprises of:

1. Preparation of 2-phenyl-4-benzoxazinone [26] (1).

2. Preparation of 4-(4-oxo-2-phenylquinazolin-3(4*H*)-yl) benzoyl chloride [27] (2).

3. Preparation of 4-(4-oxo-2-phenylquinazolin-3(4*H*)-yl) benzohydrazide [26, 28](3).

4. Cyclization to 1,3,4-oxadiazole [29](4a-4i).

5. The synthesis of oxadiazole thiones [26, 30] (5).

6. The synthesis of oxadiazole thione derivatives [31] (6).

Step 1: General procedure for the synthesis of 2-substituted-4-benzoxazinone (1): To a cold solution of anthranilic acid 0.1 moles (13.71 g) in pyridine 60 ml, p-amino benzoyl chloride 0.1 mole (15.55 g) was added. The mixture was stirred for half an hrs. Then poured into 250 ml of ice-cold water, then to it 2-3 drops of concentrated HCl was added. The resulting solid was recrystallized by ethanol. Yield: 95% M.P.: 120 ºC.

Step 2: General procedure for the synthesis of 4-(4-oxo-2-subs quinazoline-3(4*H*)-yl) benzoyl chloride (2): A mixture of compound (1) 0.05 mole (11.9 g) and *p*-amino benzoyl chloride 0.05 mole (7.78 g) in dry pyridine 50 ml was refluxed for 8 h. The resultant solution was cooled and poured into ice-cold water 100 ml containing 5 ml concentration HCl. Solid which was separated, washed with water and recrystallized by ethanol. Yield: 70.53%. M.P.: 168 ºC.

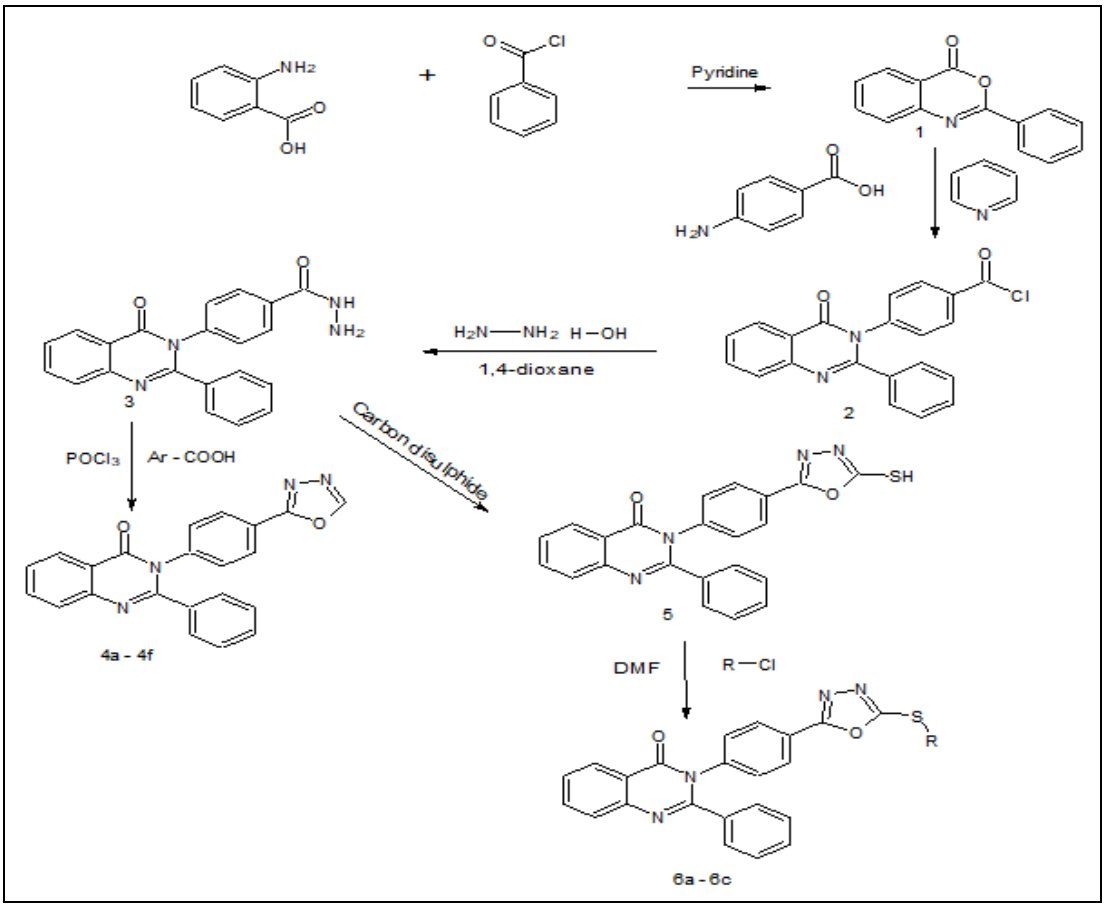
Step 3: General procedure for the synthesis of 4-(4-oxo-2-subs quinazoline-3(4*H*)-yl) benzohydrazide (3): To compound 2 (3.76 g, 0.01 mol) in 1,4-dioxane added to hydrazine hydrate (0.011 mol, 1.6 g) in 10 ml of 0.1N NaOH. Reflux it for 6 h. The reaction mixture was poured to 1N HCl. Solid thus separated by filtration and recrystallized by ethanol. Yield: 68.00%. M.P.: 150-153 ºC.

Step 4: General procedure for cyclization to 1,3,4-oxadiazole (4a-4f): The compound 3 (0.01 mole) was dissolved in $POCl_3$ (5 ml) and different aromatic acids (0.01 mole) were added. The reaction mixture after refluxing for 4-8 h was cooled to room temperature and poured onto crushed ice. On neutralization of content with neutral 20% sodium bicarbonate solution, solid separated was filtered, washed with water and dried. Ethanol and DMF recrystallized the crude product.

Step 5: General procedure for the synthesis of oxadiazole thiones (5): To compound 3 (0.01 mole) in CS_2 (0.01 mole) was refluxed for 5 h. The resultant mixture was added to ice-cold water. Then solid separated was filtered and recrystallize by ethanol. Yield: 87.57 %. M.P.: 197 ºC.

Step 6: General procedure for the synthesis of oxadiazole thiones derivatives (6a-c): To the solution of oxadiazole thiones (5) 0.01 mole in DMF (5 ml), alkyl/aryl halides 0.01 mole is added. Then the excess of DMF was evaporated to get solid substance and recrystallized by ethanol.

- **General procedure for the synthesis of *p*-amino benzoyl chloride:** Firstly *p*-amino benzoyl chloride was synthesized. 1 g of PABA was dissolved into methanol to it 2.5 ml of thionyl chloride (excess) added dropwise and shook for 20 min and kept at reflux for 2 hrs. Then solid thus separated was filtered and recrystallize by ethanol.



SCHEME 1: THE SYNTHESIS OF 1,3,4 OXADIAZOLE DERIVATIVES

TABLE 1: 3- {[2- (SUBSTITUTED-PHENYL)- 1,3,4-OXADIAZOL-2-YL] PHENYL}-3*H*-2-PHENYL-QUINAZOL-4-ONE (4A-4F)

Compound no.	Various aromatic acid
4a	Benzoic acid
4b	*p*-Cl- benzoic acid
4c	*o* -Cl- benzoic acid
4d	Cinnamic acid
4e	*p*-NH_2-benzoic acid
4f	Chloroacetic acid

TABLE 2: 2- PHENYL- 3- [4- (5-SUBSTITUTED-THIOXO-4,5-DIHYDRO-1,3,4-OXADIAZOL-2-YL) PHENYL] QUINAZOLONE (6A-6C)

Compound No	Various R_1-Cl group
6a	chlorobenzene
6b	*p*-Cl- benzoic acid
6c	*o*-Cl-benzoic acid

4a: 3- [4- (5-phenyl-1,3,4-oxadiazol-2yl) phenyl] 3*H*- 2- phenyl- quinazolin- 4(3*H*)- one: Brown coloured solid, soluble in DMSO, Molecular formula: $C_{28}H_{18}N_4O_2$. Molecular weight: 442, yield: 76.72%, M.P.: 255 ºC, solvent system TLC: Chloroform: Ethyl Acetate (1:0.1), R_f value: 0.90, IR (KBr, cm^{-1}): 2466.75 (C-H Str. for aromatic), 1712.28 (C=O Str. for quinazoline), 1609.05 (C=C Str. for aromatic), 1503.66 (C-N Str.), ^{1}H-NMR (DMSO-d_6): 7.2 -8.3 m(18-H, Ar-H), Mass spectra: 442.56 [M^+], 419.35, 372.89, 320.00, 276.55, 209.99, 155.44, 75.33. Elemental analysis % found (% calculated): C 76.13 (76.01); H 4.23 (4.07); N 12.89 (12.66).

4b: 3-{4-[5-(4-chlorophenyl)- 1, 3, 4-oxadiazol-2-yl] phenyl} 2- phenyl- quinazolin- 4(3*H*)- one: Brown coloured solid, soluble in DMSO, Molecular formula: $C_{28}H_{17}N_4O_2Cl$. Molecular weight: 477.5, yield: 76%, M.P.: 182 ºC solvent system TLC: Ethyl Acetate, R_f value: 0.93, IR (KBr,cm^{-1}): 2561.75 (C-H Str. for aromatic), 1714.48 (C=O Str. for quinazoline), 1608.48 (C=N Str. for aromatic), 1509.65 (C=C Str.), 759.99 (C-Cl Str.), 1295.68 (Str. for C-O), ^{1}H-NMR (DMSO-d_6): 7.1 -8.2 m (17-H, Ar-H), Mass spectra: 477.91 [M+1], 429.24, 371.78, 325.01, 276.59, 234.65, 209.48, 193.09, 91.33. Elemental analysis % found (% calculated): C 76-98 (76.92); H 4.51 (4.27); N 12.01 (11.96).

4c: 3- {4-[5-(2-chlorophenyl)- 1, 3, 4-oxadiazol-2-yl] phenyl} 2- phenyl-quinazolin- 4(3*H*)- one: Yellow solid compound, soluble in DMSO, Molecular formula: $C_{28}H_{17}N_4O_2Cl$. Molecular weight: 477.5, yield: 69%, M.P.: 113 ºC solvent system TLC: Ethyl Acetate, R_f value: 0.89, IR (KBr, cm^{-1}): 2569.75 (C-H Str. for aromatic), 1724.48 (C=O Str. for quinazoline), 1608.48 (C=N Str. for aromatic), 1509.65 (C=C Str.), 759.99 (C-Cl Str.), 1295.68 (Str. for C-O), ^{1}H-NMR (DMSO-d_6): 7.3-8.1 m (17-H, Ar-H), Mass spectra: 477.59 [M+1], 428.24, 370.78, 328.11, 276.59, 237.85, 209.48, 194.19, 91.41. Elemental analysis % found (% calculated): C 76-98 (76.92); H 4.51 (4.27); N 12.01 (11.96).

4d: (2*E*)- 3- (4- {5-[4-(4-oxo-2-phenylquinazolin-3(4*H*)-2yl) phenyl]-1,3,4-oxadiazol-2-yl} phenyl) prop-2-enoic acid: Light brown solid compound, soluble in chloroform, 1,4-dioxane, Molecular formula: $C_{31}H_{20}N_4O_4$, Molecular weight: 512, yield: 75%, M.P.: 155 ºC solvent system TLC: Ethyl Acetate R_f value: 0.73, IR (KBr, cm^{-1}): 2579.15 (C-H Str. for aromatic), 1731.28 (C=O Str. for quinazoline), 1609.63 (C=N Str. for aromatic), 1519.10 (C=C Str.), 2759.99 (C-OH Str.), 1295.68 (Str. for C-O), 1630.27 (aliphatic C=C), 1720.09 (C=O for acidic), ^{1}H-NMR (DMSO-d_6): 8.9, 7.0 (d, J=1.8, J=1.5, 2H, CH=CH-), 7.25-8.00 (m, 18-H, Ar-H), Mass spectra:512.44 [M+1], 415.44, 372.18, 324.89, 271.10, 276.85, 209.19, 193.63, 59.19. Elemental analysis, % found (% calculated): C 70.59 (70.51); H 3.71(3.56); N 11.53 (11.25).

4e: 3- {[2-(*p*-aminophenyl)- 1,3,4-oxadiazol-2-yl] phenyl}- 3*H*- 2-phenyl- quinazol- 4- one: Yellow solid, soluble in DMSO, Molecular formula: $C_{28}H_{19}N_5O_2$, Molecular weight: 457, yield: 89%, M.P.: 195 ºC solvent system TLC: Benzene: Chloroform (9:1), R_f value: 0.48, IR (KBr, cm^{-1}): 3408.24 (Str. primary NH_2), 3133.59 (C-H Str. for aromatic), 1711.48 (C=O Str. for quinazoline), 1608.48 (C=N Str. for aromatic), 1509.65 (C=C Str.), 1295.06 (Str. for C-O), ^{1}H-NMR ($CDCl_3$-d): 8.3 (m,17-H, Ar-H), 3.3 (t, 2H, Ar-NH_2) Mass spectra: 457.22 [M^+], 419.72, 372.78, 320.00, 276.55, 209.02, 193.09, 77.24. Elemental analysis % found (% calculated): C 73.76 (73.36); H 4.70 (4.36); N 15.58 (15.28).

4f: 3- {[2-(*p*-chloromethyl)- 1,3,4-oxadiazol-2-yl] phenyl}- 3*H*- 2- phenyl- quinazol- 4- one: Yellow solid, soluble in DMSO, Molecular formula: $C_{23}H_{15}N_4O_2Cl$, Molecular weight: 414.5, yield: 70%, M.P.: 203 ºC solvent system TLC: Chloroform: Ethyl Acetate (9:1), R_f value: 0.85, IR (KBr,cm^{-1}): 3128.10 (C-H Str. for aromatic), 1701.40 (C=O Str. for quinazoline), 1613.29 (C=N Str. for aromatic), 1517.20 (C=C Str.), 1215.10 (Str. for C-O), 725.39 (str. for C-Cl), ^{1}H-NMR ($DMSO_6$-d_6): 7.3-8.2 (m,13-H, Ar-H), 3.8 (d,J=3.8, 2H, -CH_2-Cl) Mass spectra: 415.22 [M^+], 365.19, 323.93, 271.45, 210.15, 190.23, 49.24. Elemental analysis % found (% calculated): C 66.89 (66.58); H 3.87 (3.51); N 14.17 (14.07).

5: 2- phenyl- 3- [4- (5-thioxo-5-dihydro- 1, 3, 4-oxadiazol-2-yl) phenyl] quinazolin- 4- one: Mol. Wt.: 398, Colorless solid, Soluble in DMSO, DMF, Mol. Formula: $C_{22}H_{14}N_4O_2S$, Yield: 87.57%, M.P.: 197 ºC, TLC: Ethyl Acetate: Glacial acetic acid

(1:0.1). R_f value: 0.81, IR (KBr, cm^{-1}): 3750.45 (Str. for Sec amine), 3135.52 (C-H str. for aromatic), 1708.48 (C=O Str. for quinazoline), 1622.84 (C=C Str. for aromatic), 1509.84 (C=N Str.), 1135.78 (Str. for C-S), ^{1}H-NMR ($DMSO_6$-d_6): 7.1-8.5 (m,18-H, Ar-H), 4.3(d,1H,SH). Mass Spectra: 398.56 [M^+], 371.30, 325.01, 276.59, 234.65, 209.48, 91.06, 43.31. Elemental analysis % found (% calculated): C 66.76 (66.33); H 3.59 (3.51); N 14.11 (14.07).

6a: 3- {4-[5-(phenylsuphanyl)1, 3, 4-oxadiazol-2-yl]phenyl}2-phenyl-quinazolin-4-(3*H*)-one: Light brown solid, Soluble in DMSO, Chloroform, Molecular Formula: $C_{28}H_{18}N_4O_2S$, Molecular Weight: 474, Yield: 92.5%, M.P.: 155 ºC, TLC: Chloroform: Glacial acetic acid (1: 0.1), R_f value: 0.83, IR (KBr,cm^{-1}): 2574.21 (C-H Str. for aromatic), 1718.48 (C=O Str. for quinazoline), 1652.14 (C=C Str. for aromatic), 1509.11 (C=N Str.), 1141.68 (C-S Str.) 7.4-8.3 (m,18-H, Ar-H), Elemental analysis % found (% calculated): C 70.94 (70.88); H 3.97 (3.79); N 11.89 (11.81).

6b: 3-(4-{5-[(4-chlorophenyl)sulphanyl]- 1, 3, 4-oxadiazol-2yl} phenyl) 2- phenyl-quinazolin-4(3*H*)-one: Colorless solid, soluble in DMSO, DMF, Molecular Formula: $C_{28}H_{17}N_4O_2SCl$, Molecular Weight: 508.5, Yield: 78.5%, M.P.: 159-161 ºC, TLC: Chloroform: Glacial acetic acid (1: 0.1), R_f value: 0.71, IR (KBr,cm^{-1}): 2574.21 (C-H Str. for aromatic), 1710.18 (C=O Str. for quinazoline), 1630.10 (C=C Str. for aromatic), 1501.78 (C=N Str.), 1151.28 (C-S Str.), 751.09 (C-Cl Str.), 7.1-8.3 (m,17-H, Ar-H IR (KBr,cm^{-1}): C 67.99 (67.96); H 3.61 (3.47); N 10.99 (10.81).

6c: 3-(4-{5-[(2-chlorophenyl)-sulphanyl]-1, 3, 4-oxadiazol-2yl} phenyl) 2- phenyl- quinazolin-4(3*H*)-one: Colorless solid, Soluble in DMSO, DMF, Molecular Formula: $C_{28}H_{17}N_4O_2SCl$, Molecular Weight: 508.5, Yield: 69.79%, M.P.: 149-152 ºC, TLC: Chloroform: Glacial acetic acid (1: 0.1), R_f value: 0.63, IR (KBr, cm^{-1}): 2571.20 (C-H Str. for aromatic), 1717.48 (C=O Str. for quinazoline), 1643.14 (C=C Str. for aromatic), 1503.45 (C=N Str.), 1051.56 (C-S Str.), 750.13 (C-Cl Str.), 7.2-8.1 (m,17-H, Ar-H), Elemental analysis % found (% calculated): C 68.01 (67.96); H 3.76 (3.47); N 0.89 (10.81).

Antimicrobial Activity: The newly synthesized compounds were tested *in-vitro* for their antibacterial activity against four microorganisms *viz. Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia* at 200 and 300 µg/ml concentration using the ciprofloxacin reference standard and antifungal activity against two microorganisms *Candida albicans* and *Asparagus niger* at 100 and 200 µg/ml concentration using the Fluconazole as the reference standard. Zone of inhibition at different concentration was determined by the cup-plate method.

Stock solutions (10 mg/ml) of synthesized compounds were prepared by dissolving each compound in dimethylsulfoxide. Using a standard procedure the subculture, base layer medium, agar medium, and peptone water were performed. Discs are having a measurement of 8 mm in diameter were punched from Whatman no. 1 filter paper. The test compounds were prepared in different concentrations using dimethylsulfoxide (DMSO). Solutions of the test compounds were prepared. Volumes of 0.05 ml and 0.1 ml of each compound were used for testing. The cups each of 9 mm diameter were made by scooping out medium with a sterilized cork borer in a Petri dish that was streaked with the organisms.

The solutions of each test compound (0.05 ml and 0.1 ml) were added separately in the cups and Petri dishes were subjected to incubate for 24 h at 37 °C. Standard drug ciprofloxacin was used at three concentrations namely 200 and 300 µg/ml for antibacterial activity. Parallel, to maintain the control group, 0.1 ml of DMSO was added, and this group did not exhibit any sign of inhibition. Zones of inhibition produced by each compound were measured (in mm) and the results of antibacterial studies are presented in **Table 3**.

The cup plate method using potato-dextrose agar medium was used for screening of antifungal activity against fungal strains, including *Asparagus niger* and *Candida albicans* using Fluconazole as standard drug. The method stated in Indian Pharmacopoeia prepared the nutrient broth medium and other subculture. DMSO was used as the control, and no sign of zone of inhibition was observed. Zone of inhibition produced by each

compound was measured in mm. The findings of antibacterial and antifungal evaluations are presented in **Table 4**.

Antioxidant Activity:

DPPH Method: The free radical scavenging activity of these compounds was measured using DPPH [29]. The test samples (10-100 µl) were mixed with 1.0 ml of DPPH solution and filled with methanol to make 4.0 ml. The absorbance of resulting solutions was measured at 517 nm using visible the spectrometer. Ascorbic acid is used as a reference compound. Lower absorbance of solutions indicates higher scavenging activity. Radical scavenging activity is expressed in the IC_{50} (µg/ml) **Table 5** after calculating inhibition percentage of free radical by samples using the following formula:

$$\% \text{ inhibition} = \{(A \text{ control} - A \text{ sample}) / (A \text{ control})\} \times 100$$

A control = absorbance of DPPH alone
A sample = absorbance of DPPH along with different samples.

TABLE 3: ANTIBACTERIAL ACTIVITY FOR SUBSTITUTED OXADIAZOLE DERIVATIVES

S. no.	Compound	Mean zone of inhibition (in mm)							
		Staphylococcus aureus		*Pseudomonas aeruginosa*		*Escherichia coli*		*Klebsiella pneumoniae*	
		200 µg	300 µg	200µg	300µg	200 µg	300 µg	200µg	300µg
01	Ciprofloxacin	29	35	20	26	24	31	19	25
02	4a	12	14	9	10	7	8	5	6
03	4b	10	12	8	8	6	6	5	6
04	4c	10	12	8	9	7	9	4	5
05	4d	13	15	9	11	10	11	7	8
06	4e	12	14	7	8	9	10	6	6
07	4f	13	14	7	9	8	9	6	7
08	5	14	16	6	8	8	10	5	6
09	6a	16	17	8	10	5	7	3	4
10	6b	15	16	9	10	6	7	5	6
11	6c	14	16	7	8	6	8	4	5

TABLE 4: ANTIFUNGAL ACTIVITY FOR SUBSTITUTED OXADIAZOLE DERIVATIVES

S. no.	Compound	Mean zone of inhibition (in mm)			
		Candida albicans		*Asparagus niger*	
		100 µg	200 µg	100 µg	200 µg
01	Fluconazole	0.10	0.12	0.13	0.18
02	4a	0.05	0.06	0.04	0.12
03	4b	0.06	0.07	0.05	0.07
04	4c	0.03	0.07	0.06	0.06
05	4d	0.04	0.08	0.07	0.08
06	4e	0.08	0.09	0.08	0.09
07	4f	0.06	0.09	0.067	0.08
08	5	0.05	0.06	0.06	0.06
09	6a	0.07	0.07	0.03	0.08
10	6b	0.06	0.06	0.06	0.06
11	6c	0.06	0.06	0.05	0.06

TABLE 5: IC_{50} VALUES FOR EVALUATED ANTIOXIDANT ASSAYS OF DIFFERENT DERIVATIVES

Compounds	IC_{50} (µg/ml)	Compounds	IC_{50} (µg/ml)
4a	45 ± 0.11	5	40 ± 0.15
4b	53 ± 0.14	6a	32 ± 0.11
4c	49 ± 0.29	6b	30 ± 0.14
4d	44 ± 0.41	6c	29 ± 0.09
4e	35 ± 0.10	**Ascorbic acid**	14/.8 ± 0.30
4f	57 ± 0.07		

RESULT AND DISCUSSION: Compounds of interest 4a-4f were obtained using 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzohydrazide 3 as starting material in reaction with different aryl acids in $POCl_3$ (reaction time varied from 5 to 8 hrs.) in four steps. Compound 5 was obtained using

4- (4-oxo- 2- phenylquinazolin- 3 (4H)- yl) benzo-hydrazide 3 as starting material in reaction with carbon disulphide for 5 h. The synthesis of oxadiazole thiones from the benzoxazinone is four step procedures.

Compounds 6a to 6c were obtained from compound 5 in reaction with different aryl-Cl groups in the presence of DMF.

Analytical and spectral data (IR, ^{1}H-NMR, MASS spectra) of all synthesized compounds were in full agreement with the proposed structure. IR of compounds was shown exact results. For compound 4e, it shows a peak at 3408 cm^{-1} for the free amino group. For compound 5, it shows a peak at 1121 cm^{-1} for (=S). For the C-Cl group of compound 4c, it shows a peak at 900 cm^{-1}. It also shows a peak for quinazoline moiety, *i.e.* 1711 (C=O), 1608.48 (C=C), 1509.65 (C=N). It is also showing peaks as oxadiazole molecule gives.

Mass spectra of compounds were taken. It gives molecular ion a peak nearly same *i.e.* 442.56 [M+] for 4a, 477.91[M+] for 4b, 457.22 [M+] for 4e and for 5, it shows 398.56 [M+]. The fragmentation pattern of the molecule indicates that it contains a quinazoline group as it shows a peak at 209.

Compound 5, 6a, 6b, 6c showed good activity; 4a, 4d, 4f, 4e showed moderate activity; compound 4b and 4c showed less activity against *S. aureus*. Compounds 4a, 4d, 6b showed good activity; 4b, 4c, 4e, 6a, 6c showed moderate activity; while compound 5 showed less activity towards *P. aureogenosa*. Compound 4d and 4c showed good activity, but compounds 4b, 6c, 6a, 6b showed less activity towards *E. coli*. Compounds 4d, 4e, 4f showed good activity while 4c, 6a, 6c showed less activity towards *K. pneumonia.*

In the case of antifungal activity, compound 4e showed good activity towards both strains while compounds 6b and (6c showed less activity. Compound 4a has moderate activity.

In the case of antioxidant activity compounds 6a, 6b and 6c showed better activity as compared to other derivatives.

CONCLUSION: In summary, novel conjugates between 1,3,4-oxadiazole and quinazolone were synthesized by a conventional method. Their antimicrobial and antioxidant activities were studied. The compound did not demonstrate any significant activity. Several derivatives showed slight or moderate activities. Transformation of hydrazides into 1,3,4-oxadiazole in side chain caused the dramatic loss of antiradical activity.

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CONFLICT OF INTEREST: Nil

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