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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME NOVEL 2, 3-DISUBSTITUED QUINAZOLIN-4-(3H)-ONES

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Abstract

A new series of 2, 3-disubstituted quinazolin4(3H)one derivatives was synthesized in good yield with the use of different aldehydes and evaluate their antimicrobial and anti-inflammatory activities. Disubstituted quinazolin4(3H)one derivatives were synthesized from Semicarbazide Hydrochloride and semicarbazone as starting materials through oxadiazole as intermediates. This intermediate on reaction with benoxazinone in acidic media, finally converted into corresponding 2, 3-disubstituted quinazolinone derivatives. The synthesized compounds were characterized by their physical properties, Infra-red (IR), nuclear magnetic resonance (NMR), Mass spectroscopic (MS) and elemental analysis and evaluated for biological activities. Ten different analogues of 2, 3-disubstituted quinazolin4(3H)one were successfully synthesized. All the compounds were active against microbial growth and inflammation. They all give good to moderate result on comparison with standard drug. The results reveal that pharmacological activity of quinazolin4(3H)one nucleus can be increased much times on chemical modification. This is advantageous to approaching the treatment of different kinds of severe diseases.

Keywords: Quinazoline; Oxadiazole; Quinazolin4(3H)One; Antimicrobial; Anti-Inflammatory.

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1. Introduction

It is well documentated that several bacteria and fungi pathogens have developed antibiotic resistance to various classes of antibiotics since past 30 years. The over use of antimicrobial drugs in clinical practice is one of the major factor for drug resistance. In view of the rapid increase in the multi-drug resistant (MDR) strains of pathogens, the need to search for new

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antimaicrobial drug targets has been initiated via genomics, improving existing antibiotics and by identifying new antibacterial agents with novel structure and mode of action [1,2]. In the present context, Quinazolinone nucleus (Fig.1) present in many biologically active compounds is known to posses anticancer [3, 4] antibacterial [5], antitubercular [6], antifungal [7], anthelmintic [8], anti-HIV [9], anti-inflammatory [10], antitumor [11], antihypertensive activities [12], anti-proliferative [13], antiulcer [14] and inhibitory effects for thymidylate synthase [15].

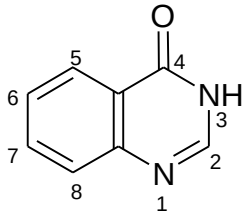

Figure 1: Structure of Quinazolinone

Owing to the biological implication of these classes of compounds, we synthesized a series of 4-(3H)-quinazoliones containing substituted styryl group at C-2 position & oxadiazoles at C-3 position and screened for antimicrobial by cup plate agar diffusion method and the zone of inhibition for each micro-organism at different concentrations and anti-inflammatory activities.

2. Materials and Methods

2.1. Material and Instruments

The purity of the synthesized compounds were ascertained by thin layer chromatography on silica gel G in various solvent systems using iodine vapours as detecting agent. Melting points of the synthesized compounds were determined using Digital Melting point Apparatus. The chemical reactions evolution was monitored on silica gel G coated TLC plates in the benzene-ethanol (8:2) solvent system. Compounds on TLC were spotted by exposing them to iodine vapors or under UV light. The IR spectra of the title compounds **(**in KBr pellets**)** were recorded on FT-IR Cary 60 spectrophotometer (Agilent Technologies, USA). 1H spectra of all the prepared compounds were recorded on a NMR spectroscopy (Bruker DPX-300 MHz) in $CDCl_3$; chemical shift (d) values are reported in parts per million (ppm). Mass spectra of the synthesized compounds were recorded on LCMS/MS (Applied Bio-system, USA). The Carlo Erba 1106 C, H, N Analyzer was used for elemental analysis of the compounds. All chemicals and reagents were purchased from Aldrich (USA) and Spectrochem Pvt. Ltd (India) and were used without further purification.

2.2. Chemistry

1,3,4-oxadiazole (**3**) was synthesized with the interaction of semicarbazone & sodium acetate in presence of glacial acetic acid and bromine. Then fused it with benzoxazinone by refluxed under anhydrous condition for 4 hrs to obtain intermediate compound 2-methy-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (**5**) [16]. The final compounds (**6a-6j**) were synthesized by the reaction of intermediate **5** with different aromatic aldehydes.

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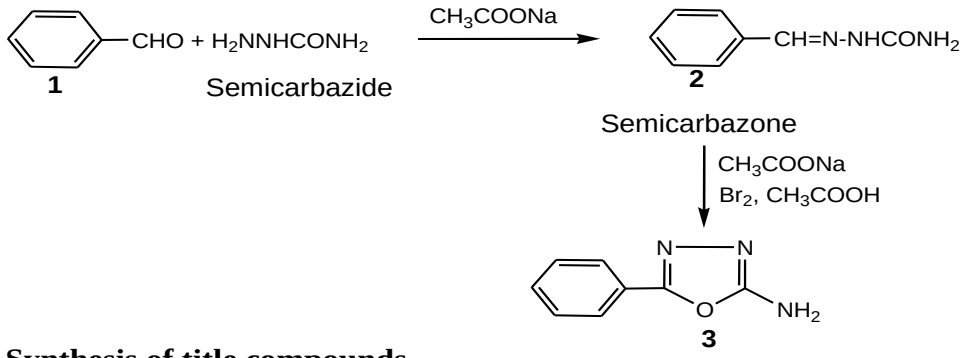
General procedure for synthesis of 3-[5-phenyl-1,3,4-oxadiazole-2-yl]-2-(substituted styryl)-quinazoline-4(3H)-ones 6(a-j)

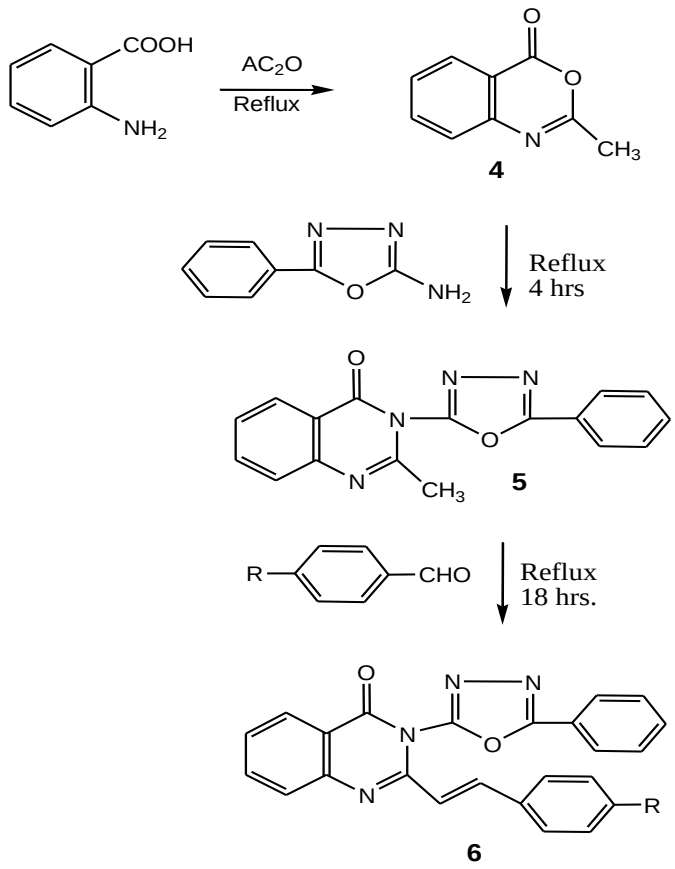
Synthetic pathway for preparation of title compounds ***6(a-j)*** is shown in Scheme-1.

Scheme for Synthesis

Synthesis of 1,3,4-Oxadiazoles



Synthesis of title compounds



Scheme 1: Scheme of synthesis of 3-[5-phenyl-1,3,4-oxadiazole-2-yl]-2-(substituted styryl)-quinazoline-4(3H)-ones

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Synthesis of 4- substituted benzaldehyde semicarbazon (2)

Semicarbazide Hydrochloride (1g) and sodium acetate (2g) were dissolved in 100 mL of distilled water placed in flat-bottomed flask. In a separate beaker, benzaldehyde (2mL) was dissolved in aldehyde free alcohol. This ethanol mixed aromatic aldehyde solution was added slowly to the solution of semicarbazide hydrochloride. The precipitate, which gets separated, was filtered, dried and recrystallised from 95% hot ethanol.

Synthesis of 2-amino -5- phenyl -1,3,4 –oxadiazole (3)

Semicarbazone (**2**) (1.5g) and sodium acetate (3g) was dissolved in glacial acetic acid (300-400 mL) with continuous stirring. Bromine (7 mL in 50 mL of glacial acetic acid) was added slowly to it. Then solution was stirred for an hour and then poured on crushed ice. The resultant solid was filtered, washed with cold water, dried and recrystallised from hot ethanol (95%).

Synthesis of 2-Methyl benzoxazin -4(3H)-one (4)

In acetic anhydride, anthracitic acid (1g) was taken and refluxed under anhydrous conditions for 4 hrs. Then distilled off the excess of acetic anhydride under reduced pressure.

Synthesis of 2-methy-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (5)

To the mixture of benzoxazinone (**4)**, 2-Amino-5-phenyl -1,3,4-oxadiazole **3** (1g) in 50 mL of glacial acetic acid was added and refluxed under anhydrous condition for 4 hrs. Then cooled and poured it into crushed ice. The solid separated out was filtered thoroughly washed with cold distilled water, dried and recrystallised from hot ethanol (95%).

Synthesis of 3-[5-phenyl-1,3,4-oxadiazole-2-yl]-2-(substituted styryl)-quinazoline-4(3H)-ones (6a-6j)

The title compounds were synthesized as per procedure reported earlier [17]. Equimolar amounts (0.01M) of intermediate compound **5** and the substituted benzaldehydes were reacted in glacial acetic (5.2mL) and refluxed for 18 hrs. The solid which separated was filtered with suction and recrystallized from hot ethanol (95%). By adopting similar type of procedures, ten compounds **6(a-j)** were synthesized. Physical and analytical data of synthesized compounds is given in Table 1 and different aldehydes which were used to prepare derivatives are shown in Table 2.

Table 1: Physicochemical properties of 2-methyl-3-[5 phenyl-1,3,4-oxadiazole-2-yl]-quinazoline-4(3h)-one derivatives

compounds	R	Molecular formula	Molecular weight	Melting Point(^{o}c)	Yield (%)	Rf value
6a.	H	$C_{24}H_{16}N_4O_2$	392.4	210	47.29	0.62
6b.	NO_2	$C_{24}H_{15}N_5O_4$	437.4	240	43.74	0.68
6c.	OH	$C_{24}H_{16}N_4O_3$	408.4	238	37.09	0.65
6d.	F	$C_{24}H_{15}FN_4O_2$	410.4	203	32.18	0.71
6e.	Br	$C_{24}H_{15}BrN_4O_2$	471.31	235	33.5	0.77
6f.	I	$C_{24}H_{15}IN_4O_2$	518.31	257	40.65	0.63
6g.	OCH_3	$C_{25}H_{18}N_4O_3$	422.44	223	44.20	0.66
6h.	$(OCH_3)_2$	$C_{26}H_{20}N_4O_4$	452.5	215	36.5	0.71
6i.	CH_3	$C_{26}H_{20}N_4O_2$	420.46	210-212	37.40	0.63
6j.	NH_2	$C_{24}H_{17}N_5O_2$	407.42	218	38.60	0.64

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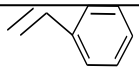
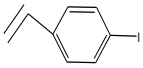
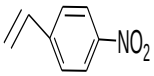
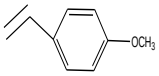
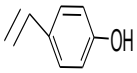
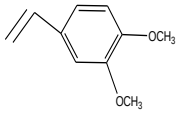
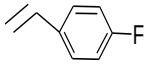
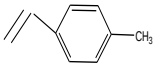
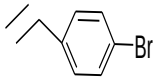
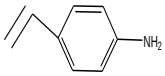
Table 2: Derivatives of synthesized compounds

S.No.	Compound	R	S.No.	compound	R
1.	6a		6.	6f	
2.	6b		7.	6g	
3.	6c		8.	6h	
4.	6d		9.	6i	
5.	6e		10.	6j	

2.3. Spectral Data of Synthesized Compounds

2-amino -5- phenyl -1,3,4 –oxadiazole (3)
IR-1348 (C-N Stretch), 3155(C-H Stretch), 1633(C=C Aliphatic Stretch), 1677 (C=O stretch). ^{1}H NMR- 4.0(Ar C-NH), 7.22 (CH), 7.48(CH), 7.32(CH). Mass-161.1(M+H). Elemental analysis($C_8H_7N_3O$)- C: 59.62, H: 4.38, N: 26.07, found C: 58.98, H: 5.06, N: 25.67. Yeild-51.53%.

2-Methyl benzoxazin -4(3H)-one (4)
IR-1394 (C-N Stretch), 3085(C-H Stretch), 1650(C=C Aliphatic Stretch), 1707 (C=O stretch). ^{1}H NMR- 7.5(CH), 7.6(CH), 8.1(CH), 0.9(CH_3). Mass-161.1(M+H). Elemental analysis($C_9H_7NO_2$)- C: 67.07, H:4.38, N: 8.69 found C: 66.83, H:5.38, N: 8.03. Yeild-48.54%.

2-methy-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one(5)
IR- 1242(C-N Stretch), 1631 (C=C Aliphatic Stretch), 1625(C=N Ring Stretch), 1670 (C=O stretch). ^{1}H NMR- 2.35, 25.0, 7.48, 7.32, 7.22. Mass- 320.1(M+H). Elemental analysis($C18H_{16}N_4O_2$)- C: 67.49, H:5.03, N:17.48, found C:65.33, H:5.44, N: 17.12. Yeild-53.31%.

2-styryl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)- quinazolin-4(3H)-one (6a)
IR- 1221(C-N Stretch), 1657 (C=C Aliphatic Stretch), 1673 (C=O stretch), 3103(C-H Stretch), 1594(C=N Stretch). ^{1}H NMR- 7.30(s, 1H, H6), 7.21(*J* = 8.0, 2.0 Hz, 1H), 7.14 (s, 1H, H5), 7.48 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.6 (m, 7H, ArH). Mass-393.1(M+H). Elemental analysis ($C_{24}H_{16}N_4O_2$)-C: 63.45, H:6.53, N:8.53, found C:63.39, H:6.51, N: 8.50. Yeild-47.29%.

2-(4-nitrostyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6b)
IR- 1521,1346 (Ar-C-NO_2 Stretch), 1315 (C-N Stretch), 1673(C=C Aliphatic Stretch), 1652(C=O stretch), 3066(C-H Stretch), 1601(C=N Ring Stretch) ^{1}H NMR- 7.56(t, *J* = 6.9 Hz,

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1H), 8.14(m, 2H), 7.32(d, 1H *J* = 8.0), 7.48(m, 1H), 7.22(s, 1H). Mass- 438.1 (M+H). Elemental analysis ($C_{24}H_{15}N_5O_4$)- C: 60.11, H:5.42,N:9.67, found C:59.87, H:5.24, N: 9.56. Yield- 43.74%.

2-(4-hydroxystyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6c)
IR-3460(O-H Stretch), 1238(C-N Stretch), 1669(C=C Aliphatic Stretch), 1670(C=O stretch), 3062(C-H Stretch), 1588 (C=N Ring Stretch). ^{1}H NMR- 7.13(s, 1H),, 6.68(t, *J*1 = 6.2 Hz, *J*2 = 9.3 Hz, 1H), 5.0(s, 2H), 7.48(m, 1H), 7.32(d, *J* = 8.0). Mass- 409.4 (M+H). Elemental analysis ($C_{24}H_{16}N_4O_3$)- C: 62.34, H:6.65,N:8.32, found C:61.93, H:6.43, N: 8.26. Yield-37.09%.

2-(4-fluorostyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6d)
IR- 945(Ar-C-F Stretch), 1298(C-N Stretch), 1685(C=C Aliphatic Stretch), 1665(C=O stretch), 3076(C-H Stretch), 1598(C=N Stretch). ^{1}H NMR- 7.28(s, 1H), 6.92(s, 2H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s, 1H). Mass- 409.2 (M+H). Elemental analysis($C_{24}H_{15}FN_4O_2$)- C: 65.74, H:7.52,N:8.69, found C:64.83, H:7.48, N: 8.52. Yield-32.18%.

2-(4-bromostyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6e)
IR- 562 (Ar- C-Br stretch), 1330 (Ar-C-N Stretch), 1670 (C=C Aromatic Stretch), 1682(C=O stretch), 3100 (C-H Stretch), 1590(C=N Stretch), 1092(C-O Stretch). ^{1}H NMR- 7.19(s,2H), 7.38(s,3H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s,1H) . Mass-470.4 (M+1). Elemental analysis($C_{24}H_{15}BrN_4O_2$)- C:61.20, H:3.28,N:11.89, found- C:59.2, H: 3.10,N:11.03. Yield-33.5%.

2-(4-iodostyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6f)
IR- 493(C-I stretch), 1210 (Ar-C-N Stretch), 1658 (C=C Aromatic Stretch), 1654(C=O stretch), 2937 (C-H Stretch), 1592(C=N Stretch), 1129(C-O Stretch). ^{1}H NMR- 7.07(s, 2H), 7.59(s,3H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s,1H) . Mass- 518.5 (M+1). Elemental analysis($C_{24}H_{15}IN_4O_2$)- C:55.60, H:2.94,N:10.82, found- C:55.45, H: 2.33, N:10.46. Yield-40.65%.

2-(4-methoxystyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6g)
IR- 1300 (Ar-C-N Stretch), 1673 (C=C Aromatic Stretch), 1664(C=O stretch), 3127 (C-H Stretch), 1583(C=N Stretch), 1096(C-O Stretch). ^{1}H NMR- 3.73(s, 3H), 6.72(s, 2H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s,1H) . Mass- 421.7 (M+1). Elemental analysis($C_{25}H_{18}N_4O_3$)- C:71.08, H:4.29, N:13.26, found- C:70.62, H: 3.82, N:12.75. Yield-44.20%.

2-(3,4-dimethoxystyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6h)
IR- 1350 (Ar-C-N Stretch), 1662 (C=C Aliphatic Stretch), 1678(C=O stretch),3115 (sp^2 C-H Stretch), 2937 (sp^3 C-H Stretch), 1604(C=N Stretch), 1330, 1091(C-O Stretch). ^{1}H NMR- 6.70(s,2H), 3.73(s, 3H), 7.48(m,1H), 7.32(d, J = 8.0). Mass- 453.3 (M+H). Elemental analysis($C_{26}H_{20}N_4O_4$)- C:61.70, H:5.33,N:9.22, found C:60.53, H:5.29, N: 9.10. Yield-36.50%.

2-(4-ethylstyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6i)
IR- 1451 (CH_3 stretch), 1282 (Ar-C-N Stretch), 1652 (C=C Aromatic Stretch), 1656(C=O stretch), 2995 (C-H Stretch) 1597(C=N Stretch), 1101(C-O Stretch). ^{1}H NMR-1.24(s,1H), 7.07(s,2H), 7.25(s,3H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s,1H) . Mass- 420.1 (M+1). Elemental analysis($C_{26}H_{20}N_4O_2$)- C:74.27, H:4.79, N:13.33, found- C:74.02, H: 4.12, N:13.05. Yield-37.40%.

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2-(4-aminostyryl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinazolin-4(3H)-one (6j)
IR- 3152(N-H stretch), 1350 (Ar-C-N Stretch), 1656 (C=C Aromatic Stretch), 1672(C=O stretch), 3101 (C-H Stretch), 1585(C=N Stretch), 1083(C-O Stretch). ^{1}H NMR-6.41(), 7.30(s, 1H), 7.50 (ms, 1H), 7.07(s, 2H), 7.48(m,1H), 7.32(d, J = 8.0), 7.22(s,1H) . Mass- 407.4 (M+1). Elemental analysis($C_{24}H_{17}N_5O_2$)- C:70.75, H:4.21, N:17.19, found- C:70.18, H: 3.76, N:16.34. Yield-38.60%.

2.4. Biological Evaluation

Antimicrobial Activity
Antimicrobial screening of the 3-[5-phenyl-1,3,4-oxadiazole-2-yl]-2-(substituted styryl)-quinazoline-4(3H)-ones **6(a-j)** was done following the agar well diffusion method with Mueller Hinton agar media [18-20]. All the compounds (**6a–6j**) were screened for their *in vitro* antibacterial activity against *Pseudomonas aeruginosa* (ATCC 10145), *Escherichia coli* (ATCC 25922), *Staphylococus aureus* (ATCC 10231) and *Streptococcus pyogenes* (MTCC 442) at 2500µg/mL, 250µg/mL, 25µg/mL, 2.5µg/mL, 0.25µg/mL and 0.025µg/mL with Ampicillin as the standard drug.

Antifungal activity was conducted against *Aspergillus niger*, ATCC 16888 and *Candida albicans* ATCC 24433 at 2500µg/mL, 250µg/mL, 25µg/mL, 2.5µg/mL, 0.25µg/mL and 0.025µg/mL using Miconazole as the standard drug.

The test organisms were first cultured in nutrient broth and incubated for 24 h at 37 ^{o}C and then freshly prepared bacterial cells and fungal spores were spread onto the Muller Hinton agar plates and Potato Dextrose Agar medium, respectively, in a laminar flow cabinet. The test compounds which were previously dissolved in DMF were then soaked onto sterile disks of Whatman filter paper (5 mm diameter).

The disks were then placed onto the surface of the previously prepared inoculated plates and incubated. The zone of inhibition was recorded in mm after incubation of plates for 24 hrs (antibacterial) and 72 hrs (antifungal) at 37 ^{o}C as shown in Table 3 and Table 4.

Table 3: Anti-bacterial activity of synthesized compounds

Compounds	**Bacteria**		**Diameter of zone (in mm) as per Concentration Placed in agar well (in µg/mL)**					
			2500	**250**	**25**	**2.5**	**0.25**	**0.025**
6a.	Gram -ve	*P.aeruginosa*	21	15	10	-	-	-
		E. coli	18	14	08			
	Gram +ve	*S. aureus*	20	16	10	-	-	-
		S. pyogenes	22	15	11			
	Gram	*P.aeruginosa*	25	18	12	-	-	-

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	-ve	*E. coli*	22	15	09	-	-	-
6b.	Gram +ve	*S. aureus*	23	15	16	-	-	-
		S. pyogenes	21	16	12	-	-	-
	Gram -ve	*P.aeruginosa*	20	17	12	10	-	-
		E. coli	22	15	10	-	-	-
6c.	Gram +ve	*S. aureus*	15	12	10	-	-	-
		S. pyogenes	18	13	08			
6d	Gram -ve	*P.aeruginosa*	26	17	14	-	-	-
		E. coli	27	22	16	11	-	-
	Gram +ve	*S. aureus*	18	16	12	-	-	-
		S. pyogenes	21	16	18	-	-	-
6e.	Gram -ve	*P.aeruginosa*	28	20	16	12	-	-
		E. coli	28	19	12	-	-	-
	Gram +ve	*S. aureus*	20	16	13	-	-	-
		S. pyogenes	24	17	11	-	-	-
6f.	Gram -ve	*P.aeruginosa*	28	24	19	13	-	-
		E. coli	26	21	15	-	-	-
	Gram +ve	*S. aureus*	27	22	15	10	-	-
		S. pyogenes	24	19	13	-	-	-
6g.	Gram -ve	*P.aeruginosa*	24	16	12	-	-	-
		E. coli	24	18	10	-	-	-
	Gram +ve	*S. aureus*	20	18	10	-	-	-
		S. pyogenes	22	15	08	-	-	-
6h.	Gram -ve	*P.aeruginosa*	22	19	13	-	-	-
		E. coli	18	12	-	-	-	-
	Gram +ve	*S. aureus*	23	15	10	-	-	-
		S. pyogenes	21	16	11	-	-	-
	Gram -ve	*P.aeruginosa*	23	17	12	-	-	-
		E. coli	23	15	10			

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6i.	Gram +ve	*S. aureus*	21	16	09	-	-	-
		S. pyogenes	18	11	-			
	Gram -ve	*P.aeruginosa*	20	13	10	-	-	-
		E. coli	22	15	10	-	-	-
6j.	Gram +ve	*S. aureus*	18	12	08	-	-	-
		S. pyogenes	22	18	12	-	-	-
	Gram -ve	*P.aeruginosa*	25	21	16	11	-	-
Ampiciline		*E. coli*	25	20	14	-	-	-
	Gram +ve	*S. aureus*	22	18	12	-	-	-
		S. pyogenes	24	19	13	-	-	-

(- = not active)

Table 4: Anti-fungal activity of synthesized compound

Compounds	**Fungai**	**Diameter of zone (in mm) as per Concentration Placed in agar well (in µg/mL)**					
		2500	**250**	**25**	**2.5**	**0.25**	**0.025**
6a.	A. nigar	16	13	-	-	-	-
	C. albicans	22	17	13	-	-	-
6b.	A. nigar	20	13	10	-	-	-
	C. albicans	23	15	-	-	-	-
6c.	A. nigar	23	19	13	-	-	-
	C. albicans	20	13	10	10	-	-
6d	A. nigar	18	16	12	-	-	-
	C. albicans	22	18	12	-	-	-
6e.	A. nigar	24	18	13	-	-	-
	C. albicans	26	22	17	12	-	-
6f.	A. nigar	23	17	11	-	-	-
	C. albicans	26	20	16	11	-	-
6g.	A. nigar	22	15	-	-	-	-
	C. albicans	17	14	10	-	-	-
6h.	A. nigar	20	15	12	-	-	-
	C. albicans	24	17	13	-	-	-

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6i.	A. nigar	23	17	12	-	-	-
	C. albicans	22	19	13	-	-	-
6j.	A. nigar	18	12	-	-	-	-
	C. albicans	20	16	11	-	-	-
Miconazole	A. nigar	25	19	14	-	-	-
	C. albicans	22	17	14	10	-	-

(- = not active)

Anti-inflammatory Activity

Anti-inflammatory activity of synthesize compounds was evaluated by carragenan-induced rat hind paw edema method [21]. Ibuprofen was used as a reference drug. The rats were divided into three groups (control, treated, and standard drug) of six animals each. A freshly prepared suspension of carrageenan (1% in 0.9% saline) 0.05 mn was injected under the planter aponeurosis of the right hind paw of each rat. Test compounds and standard drug were administered orally to the animals of drug-treated groups and the standard drug group, respectively, 1 h before the carragenan injection. The paw volume of each rat was measured before 1 and after 3 h of carrageenan treatment with the help of a plethysmometer. The percent anti-inflammatory activity was calculated according to the formula given below

$$\% \text{ inhibition of edema} = (1 - V_t / V_c) \times 100$$

Where V_t and V_c are the mean increase in paw volume of rats of the treated and the control group, respectively.

3. Results and Discussion

The synthesis of 3-[5-phenyl-1,3,4-oxadiazole-2-yl]-2-(substituted styryl)-quinazoline-4(3H)-ones 6(a-j) was accomplished as presented in Scheme-1. The title compounds 6(a-j) were synthesized by the reaction of 2-methyl-3-[5-phenyl-1,3,4-oxadiazole-2-yl]-quinazoline-4(3H)-one (5) with different substituted benzaldehydes. All the synthesized compounds were characterized by modern analytical techniques. The IR, NMR and mass spectra were consistent with the proposed chemical structures. The FT-IR spectrum exhibited characteristic bands for ArC-N strching, C=O stretch and CH-Ar at 1350-1221, 1682-1654 and 3127-3103 cm-1 respectively.

All the synthesized compounds were screened for antimicrobial and anti-inflammatory activities. The compounds 6f, 6e, 6d showed significant antimicrobial activity in compared to standard drugs, Ampicillin and Miconazole (Table 3 and Table 4). The results showed that presence of imino linkage (-N=C-) in the structure favours the antimicrobaial activity.

All the synthesized compounds also showed moderate anti-inflammatory activity (Table 5) as compared to standard drug ibuprofen. Compound 6f was found most active compound in series with 47.24% inhibition of edema that shows the presence of electron withdrawing group in 3rd position of Quinazolinone ring fovours the activity.

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Table 5: Anti-inflammatory activity of synthesized compounds

S.No.	Compounds	Dose (mg/kg)	% Inhibition
1.	Control	50	-
2.	Ibuprofen	50	43.43
3.	6a	50	39.57
4.	6b	50	48.62
5.	6c	50	34.55
6.	6d	50	42.50
7.	6e	50	42.76
8.	6f	50	47.24
9.	6g	50	43.62
10.	6h	50	38.28
11.	6i	50	41.08
12.	6j	50	38.64

Conflict of Interest

The authors confirm that this article content has no conflicts of interest.

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