Research Article

SYNTHESIS AND ANTIMICROBIAL STUDIES OF OXAZOLIDINONE DERIVATIVES

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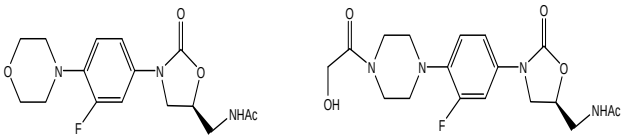
ABSTRACT

A novel approach to the synthesis of 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-chloro/nitro/methoxy benzylidene) oxazolidin-4-one 4(a-c) and 4-(6-(7-chloroquinolin-4-ylamino)hexyl) -2(4-chloro/nitro/methoxy benzylidene)-1,6-diox-4,9-diazaspiro[4,4] nonane-3,8-dione 5(a-c) has been described. Treatment of 1,6-diamino hexane with 4,7-dichloroquinoline yielded N-(7-chloroquinoline-4-yl)hexane-1,6-diamine (1). Condensation of amine with chloroacetylchloride afforded 3-(6-(7-chloroquinoline-4-yl-amino)hexyl)-2-imino-oxazolidin-4-one (3) which reacted smoothly with p substituted aldehydes to give 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-chloro/nitro/methoxy benzylidene) oxazolidin-4-one (4 a-c) in excellent yield. These imino substituted oxazolidinone (4a-c) react with glycolic acid to give spiro oxazolidin-4-one 6(a-c) derivatives. N-(7-chloroquinoline-4-yl)hexyl-1,6-diamine (1), 3-(6-(7-chloroquinoline-4-yl-amino)hexyl)-2-imino-oxazolidin-4-one (3), 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-chloro benzylidene) oxazolidin-4-one (4a) and 4-(6-(7-chloroquinolin-4-ylamino)hexyl)-2(4-methoxybenzylidene)-1,6-diox-4,9-diazaspiro[4,4]nonane-3,8-dione 5(c) were screened for their in-vitro antimicrobial activities against bacterial species *E.coli* (MTCC119) and *B.substilis* (MTCC 96)) and fungal species *A.niger* (MTCC 1344) and *C.albicans* (MTCC 871) by Agar-well assay method against the standard drugs (streptomycin for bacteria and fluconazole for fungi).

Keywords: Synthesis, Oxazolidinone, antitoxicity, antibacterial properties, antifungal properties.

INTRODUCTION

Oxazolidinones represent the first new class of antibacterial drugs in the last 35 years. Oxazolidinones are five membered heterocyclic compounds containing nitrogen and oxygen as hetero atoms. The C-2 and C-4 positions of the oxazolidinone are crucial for their various biological activities. N-substituted oxazolidinones also participated in variety of intermolecular reactions. Considering these properties, various research workers have shown a keen interest in this small heterocyclic moiety as target structure for evaluation of many pharmacological activities. Since many decades, active heterocyclic compounds are one of the main topic of interest for the medicinal chemists as it displays a number of pharmacological activities. Nitrogen, sulphur, oxygen containing five and six membered heterocyclic compounds have occupied enormous significance in the field of medicinal chemistry. Oxazolidinones[1] are heterocyclic compounds which perform an important role in the synthesis of several organic molecules including amino acids[2,3], amino alcohols[4,5], thiamine[6], amides[7,8], peptides[10] and polyfunctional compounds[11]. Certain natural and synthetic oxazolidinone derivatives possess important biological activities such as anticancer[12-14], antibacterial[15,16], antifungal[17], anticonvulsant[18], anti-inflammatory[19,20], antituberculosis[21,22], cardiotonic[23], anti-HIV[24], antidiabetic[25] and antiangiogenic activity[26]. Oxazolidinones are also important for drug development, especially in the area inhibitors of monoamine oxidase[27]. Oxazolidinones are also important for drug development, especially in the area of antibacterials[28], and inhibitors of monoamine oxidase[29]. They also have potent pharmacological effects as cytokine modulators[30], sigma receptors[31], phychotropics[32], antiallergy agents[33], antibiotics[34] and intermediates in the synthesis of rennin inhibitors[35], β-lactam and macrolide antibiotics[36], immunosupressants[37] and in various other applications[38].



Linezolid Eperezolid

Figure 1

Several derivatives of oxazolidinones have been prepared in the literature in search of the newer physiologically active materials from this nucleus. Greatly encouraged by such a concept of drug design and synthesis of oxazolidinones derivatives, it is aimed in the present work to synthesize chloroquinonline ring containing spiro-oxazolidinones derivatives. On the basis we describe the synthesis of novel spiro oxazolidinone derivatives with a view to verify this assumption that its incorporation of quinoline could really produce an additive affect on the biological properties of the parent molecule. Discussion will concerning synthesis antimicrobial properties of N-(7-chloroquinoline-4-yl)hexyl-1,6-diamine (1), 3-(6-(7-chloroquinoline-4-yl-amino)hexyl) -2-imino-oxazolidin-4-one (3), 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-chlorobenzylidene)oxazolidin-4-one (4a) and 4-(6-(7-chloroquinolin-4-ylamino)hexyl)-2(4-methoxy benzyl-idene)-1,6-diox-4,9-diazaspiro[4,4]nonane-3,8-dione 5(c).

MATERIALS AND METHODS

The entire chemicals were purchased from Aldrich Chemical Company (USA) and were used after purification by distillation. The reactions were monitored by precoated aluminium silica gel 60F 254 thin layer plates procured from Merck (Germany). All melting points were measured with a capillary apparatus and are uncorrected. All the compounds were routinely checked by IR, ^{1}H NMR and mass spectrometries. IR spectra were recorded in KBr on a Perkin–Elmer model 8201 FTIR spectrophotometer. ^{1}H NMR spectra were recorded at ambient temperature using a Brucker spectroscopin DPX-300 MHz spectrophotometer in DMSO. The following abbreviations were used to indicate the peak multiplicity s – singlet, d – doublet, t – triplet, m – multiplet. FAB mass spectra were recorded on a JEOL SX102 mass spectrometer using Argon/Xenon (6 kV, 10 mB) gas. Column chromatography was performed on silica gel (Merck). Anhydrous sodium sulfate was used as a drying agent for the organic phase.

Preparation of N-(7-chloroquinoline-4-yl)hexane-1,6-diamine (1)

A mixture of 2.97g (0.59mol) 4,7-dichloroquinoline, 30ml of distilled ethanol, 0.89g (0.07mole) of 1-6-diaminhexane was placed in a 250 ml round bottom flask and refluxed for 8h., the solid obtained was extracted with DCM in presence of brine solution. Organic layer was separated and dried with Na_2SO_4. The solvent was evaporated under reduced pressure, and the resultant solidness obtain. The solid obtained was recrystelized from EtOH and purified through the column to obtained compound (1). The characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3457, 3225 [NH str.], 3150, 2928 [C-H str.],1559 [NH str.],1485 [C-H bend], 1200 [C-N str.], 786 [C-Cl str.]. **^{1}HNMR δ** 8.1[d, 1H, Ar.H], 8.0[s, 1H, Ar.H],7.8 [d, 1H, Ar.H],7.4 [d, 1H, Ar.H],6.0 [d, 1H, Ar.H],4.9 [s, 1H, NH],2.4[s, 2H, NH_2],1.5-3.7 [m, 12H, (CH_2).]. **Mass spectra m/z** (M +1) : 277.

Preparation of 2-Chloro-N-(6-(-7-chloroquinoline-4-yl amino) hexyl) acetamide (2)

A mixture of compound N-(7-chloroquinoline-4-yl)hexane-1,6-diamine **1** (2.35g, 1ommol) and chloroacetyl chloride 0.75ml (10m.mol) dissolved in triethyl amine (1ml) and dry EtOH (25ml) were stirred for about 30 min. on ice bath then refluxed for 4-6 hr. Completion of the reaction was checked by TLC. After completion, the reaction solution was cooled and the solvent was evaporated, solid product obtained which was separated with DCM and water mixture. The organic layer was filtered and dried with Na_2SO_4. Resultant product was purified by column chromatography in silica gel G (methanol and benzene). The elutes were concentrated and the products were recrystallized from EtOH to obtain compound (2). Characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3049, 2958[C-H str.], 1720 [C=O],1606, 1562[NH (Amine)], 1486 [C-H bend], 1355[C-Nstr.], 769[C-Clstr.Aro]. **^{1}HNMR δ**8.82 [s,1H,NHCO], 8.46[s,1H,ArH], 8.09[d,1H,ArH], 7.98[d,1H,ArH], 7.17[d,1H,ArH], 6.95[d,1H,ArH], 4.51[s,1H,NH], 3.35[s,2H,CH_2], 1.21-1.89[m,12H,CH_2]. **Mass spectra m/z** calcud for $C_{17}H_{17}Cl_2N_3O$ (M +1) : 353.

Preparation of 3-(6-(7-chloroquinoline-4-yl-amino) hexyl)-2-imino-oxazolidin-4-one (3)

A mixture of compound **(3)** 2-chloro-N-(3-7-chloroquinoline-4-ylamino) hexyl) acetamide 1.66g (5mmol) dissolved in dry acetone (10ml) and potassium cyanate 0.58g (7m.mol) were kept for condensation on water bath for about 8 hr. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio. After completion of the reaction, mixture was cooled and was evaporated solid mass obtained was neutralized by standard solution of $NaHCO_3$ and dried on Na_2SO_4. The product was recrystallized with EtOH. The solvent was evaporated under reduced pressure and the resultant solid obtain (3). The characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3200,2926 [C-H str.],1715 [C=O], 1658 [C=NH (Imine)] ,1469 [NH (Amine)], 1385 [C-H bend CH_2], 1325[C-N str.], 786 [C-Cl str.(Aro)], **^{1}HNMR δ**8.86 [s,1H,NH], 8.75 [s,1H,ArH], 8.18[d,1H,ArH], 8.04[d,1H,ArH], 7.46[d,1H,ArH], 6.75[d,1H,ArH], 4.32[s,2H,CH_2], 4.10[s,1H,NH], 1.60-1.25[m,12 H,CH_2]. **Mass spectra m/z** (M +1) : 360.

Preparation of 3-(6-(7-chloroquinolin-4-ylamino) hexyl-2-imino-5-(4-chloro/nitro benzylidene) oxazolidin-4-one (4a-b)

A mixture of compound **(4.059)** 3-(6-(7-chloroquinoline-4-ylamino)propyl)-2-imino-oxazolidin-4-one 0.30 gm(0.13 mmol) and sodium acetate (0.10gm) was mixed with p-chlorobenzaldehyde 0.127 gm (0.017mmol) in dry benzene (20ml). The solution was refluxed on water bath for 8 hr. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled at room temperature and the solution was filtered, the filtrate was concentrated and purified by column chromatography the product was recrystallized with ethanol to give compound (4a). Characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3299, 2924[C-Hstr.Ar.H], 1720[C=O], 1600 [C=C str.], 1551 [NH str.], 1510 [NH str.], 1448 [C-H bend. CH_2], 1200 [C-N str.],795 [C-Cl str.]. **^{1}HNMR δ** 11.3[s,1H,(NH)], 8.65[dd,2H, ArH], 8.00[s, 1H, ArH],7.54[s,2H, C=H], 7.51[d,1H, ArH], 7.24[dd,2H,ArH], 7.21[dd,2H, ArH], 6.39[d,1H, ArH], 4.37[s,1H,(NH)], 1.26-2.89[m,12H (CH_2)]. **Mass spectra m/z** (M +1) : 482.

Similarly the product 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-nitro benzylidene)oxazolidin-4-one (4b) was synthesized using p-nitrobenzaldehyde. Characterization data are presented in **table 1.**

IR Cm^{-1} (KBr) 3058, 2945[CHstr.Ar.H], 1705[C=O], 1695 [C=C str.], 1569[NH str.(Imine)], 1494 [NH str.(Amine)], 1446 [C-H bend. CH_2], 1359[N-O str.], 1307[C-N str.], 730[C-Cl str.]. **^{1}HNMR δ** 10.35[s,1H,(NH)], 8.61[dd,2H, ArH], 8.14[dd,2H, ArH],8.05[s, 1H, ArH],7.62[dd,2H, ArH],

7.77[s,2H, C=H], 7.56[dd,1H,ArH], 6.44[d,1H, ArH], 4.13[s,1H,(NH)], 1.16-2.89[m,12H (CH_2)]. **Mass spectra m/z** (M +1) : 492.

Preparation of 3-(6-(7-chloroquinolin-4-ylamino) hexyl-2-imino-5-(4-methoxy benzylidene) oxazolidin-4-one (4c)

A mixture of compound **(3)** 3-(6-(7-chloroquinoline-4-ylamino)hexyl)-2-imino-oxazolidin-4-one 0.30 gm (0.13 mmol) and zinc chloride (0.50 mg) mixed with p-methoxybenzaldehyde 0.127 gm (0.017mmol) in glacial acetic acid (20ml). The solution was refluxed on sand bath for 8 hr at 120°C. The progress of the reaction was checked by TLC using methanol-benzene (1:9) ratio as an eluent. After completion of the reaction it was cooled at room temperature and the solution was neutralized $NaHCO_3$, white precipitate occurs which was pour in the water and filtered. The compound crystallized with methanol and water. The obtained solid purified by column chromatography the product were recrystallized with ethanol to give 3-(6-(7-chloroquinolin-4-ylaminohexyl-2-imino-5-(4-methoxy benzylidene) oxazolidin-4-one (4c)**.** The characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3278, 2876[CHstr.Ar.H], 1710[C=O], 1690 [C=C str.], 1650 [NH str.(Imine)], 1545 [NH str.(Amine)], 1468 [C-H bend. CH_2], 1355[C-N str.], 1245[C-O(Eater)] 745[C-Cl str.]. **^{1}HNMR δ**10.01[s, 1H(NH)], 8.78 [d,1H,ArH], 8.49 [d,1H,ArH], 8.18[d,1H,ArH], 8.15 [d,1H,ArH], 8.12[s, 1H, ArH], 7.84[d,1H,ArH], 7.65 [d, 1H, ArH], 7.48[d,1H,Ar], 7.71[s,2H,C=H], 6.98 [d,1H,Ar.], 4.69[s, 1H(NH)], 3.3[s, 3H (CH_3)], 1.7-1.2[m, 12H (CH_2)]. **Mass spectra m/z** (M +1) : 477

Preparation of 4-(6-(7-chloroquinolin-4-ylamino)hexyl)-2(4-nitrobenzylidene/chlorobenzylidene)-1,6-diox-4,9-diazaspiro[4,4]nonane-3,8-dione 5(a-b)

A mixture of compound **(4a)** 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-chloro benzylidene) oxazolidin-4-one 0.20gm (0.45mmol) dissolved with glycolic acid 3.37gm (0.25mmol) and dry benzene (20 ml) was condensation on water bath for about 24 hr. The completion of the reaction checked by TLC using methanol-benzene (2:8) ratio as an eluent. After completion of the reaction, it was cooled and neutralized with aqueous standard solution of sodium bicarbonate ($NaHCO_3$) and water successively and purified by column chromatography to obtain compound (5a). Characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3298[NH str.(Amine)], 3012,2978[C-H str.], 1711[C=O], 1657[C=CH],1500[NH (Amine)],1462 [C-H bend CH_2], 1245[C-N str.], 761, 665[C-Cl str.(Aro)], **^{1}HNMR δ** 8.8[s,1H,NH], 8.7[d,1H, ArH], 8.4[d,1H, ArH], 8.2[d,1H, ArH], 8.1[s, 1H, Ar.H], 8.0[d,1H, ArH], 7.4-7.5[m,3H, ArH], 6.9[d,1H, ArH], 6.7[s, 2H, (C=H)], 3.8[s,1H,NH], 3.3[s,2H, ($Ar.CH_2$)],1.5-1.0[m,12H (CH_2)]. **Mass spectra m/z** (M +1) : 540

Similarly the product 4-(6-(7-chloroquinolin-4-ylamino)hexyl)-2(4- nitrobenzylidene) -1,6-diox-4,9-diazaspiro[4,4] nonane-3,8-dione **(**5b) was synthesized using of compound 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-nitro benzylidene)oxazolidin-4-one **(4b)** 3.37gm. Characterization data are presented in **table 1. IR Cm^{-1} (KBr)** 3221[NH str.(Amine)], 3022,2941[C-H str.], 1718[C=O(str.)], 1659[C=CH], 1505[NH (Amine)], 1345[N-O], 1485 [C-H bend CH_2], 1232[C-N str.], 762[C-Cl str.(Aro)]. **^{1}HNMR δ** 8.8[s,1H,NH], 8.6[d,1H, ArH], 8.1[dd,2H, ArH], 8.0[s, 1H, Ar.H], 7.6[d,1H, ArH], 7.5[dd,2H, ArH], 7.3[d,1H, ArH], 6.4[d,1H, ArH], 5.9[s, 2H, (C=H)], 4.3[s,2H, ($Ar.CH_2$)], 4.1[s,1H,NH], 2.9-1.5[m,12H (CH_2)]. **Mass spectra m/z** (M +1) : 493.

Preparation of 4-(6-(7-chloroquinolin-4-ylamino) hexyl)-2(4-methoxybenzylidene)-1,6-diox-4,9-diazaspiro[4,4] nonane-3,8-dione 5(c)

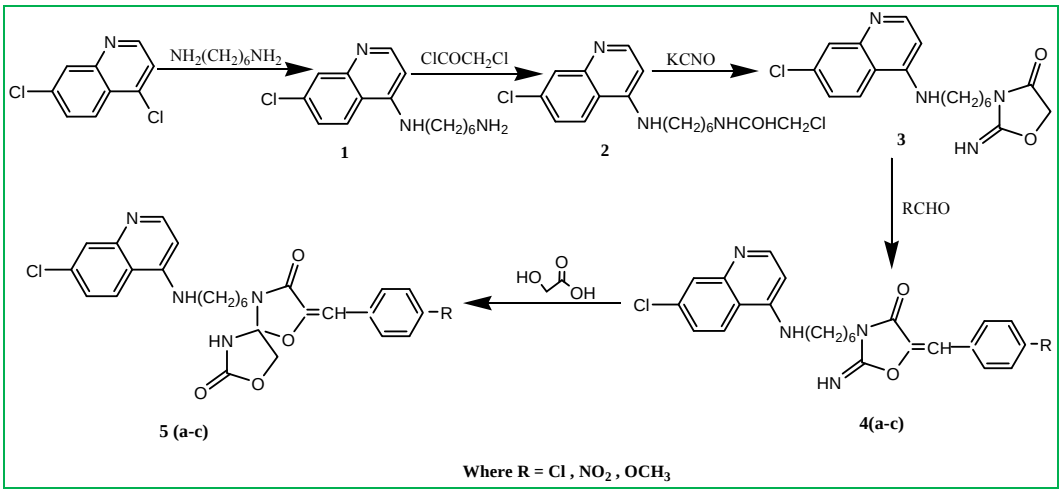
A mixture of compound **(5.049)** 3-(6-(7-chloroquinolin-4-ylamino)hexyl-2-imino-5-(4-methoxy benzylidene) oxazolidin-4-one 0.30gm (0.12mmol) mixed with zinc chloride (0.50 mg) and glycolic acid 3.37gm (0.25mmol) and dissolved in glacial acetic acid (20 ml) were reflux on sand bath for about 6-7 hr. The temperature of the reaction mixture was raised to 120°C and maintained at the same temperature. The completion of the reaction checked by TLC using methanol-benzene (2:8) ratio as an eluent. After completion of the reaction, it was cooled and neutralized with ammonium hydroxide and purified by column chromatography to obtain 4-(6-(7-chloroquinolin-4-ylamino)hexyl)-2(4-methoxy benzylidene) -1,6-diox-4,9-diazaspiro[4,4]nonane-3,8-dione 5(c). Characterization data are presented in **table I. IR Cm^{-1} (KBr)** 3246[NH str.(Amine)], 3027,2978[C-H str.], 1720[C=O(str.)], 1656[C=CH],1521[NH (Amine)], 1464[C-H bend CH_2], 1333[C-N str.], 1300[C-O(str.)], 766[C-Cl str.(Aro)]. **^{1}HNMRδ** 9.8[s,1H,NH], 8.7[d,1H, ArH], 8.2[d,1H, ArH], 8.0[s, 1H, Ar.H], 7.8[d,1H, ArH], 7.5[d,1H, ArH], 7.2[s, 2H, (C=H)], 6.9[d,1H, ArH], 6.8-7.2[m,3H, ArH], 4.0[s,1H,NH], 3.8[s,3H, (CH_3)],3.1[s,2H, ($Ar.CH_2$)], 1.6-1.1[m,12H (CH_2)]. **Mass spectra m/z** (M +1) : 536.

RESULTS AND DISCUSSION

Chemistry

A new synthetic method for the preparation of oxazolidinone has been developed and obtained the desired oxazolidinone derivatives in 54-80% yields. All the nine compounds were prepared by refluxing in the presence of solvent (dry ethanol, acetone and benzene). The obtained compounds are stable in the solid state. Characteristic IR bands provide significant indications for the formation of oxazolidinone derivatives. IR spectra of all the compounds showed 1500-1578 cm^{-1} (NH str.), 1735-1770 cm^{-1} (C=O str.), 1600-1475 cm^{-1}(C=C str.), which confirmed the formation of oxazolidinone derivatives. The structure of oxazolidinone derivatives were further confirmed by ^{1}H-NMR spectra, which proves as a diagnostic tool for the positional elucidation of the proton. Assignments of the signals are based on chemical shift and intensity pattern. The^{1}H-NMR spectra showed multiplets in the region 1.5-2.0 ppm for (CH_2) and doublets in the region 8.14-7.3 ppm for aromatic proton

in all spectra respectively, details are given in experimental section. Characteristic peaks were observed in the mass spectra of all compounds which followed the similar fragmentation pattern. The spectra of compounds showed molecular ion peak (M^+) at m/z which confirmed the molecular weight of the oxazolidinone derivatives.



Scheme - 1

Table 1: Physical Data of Synthesized Compounds

Comp	Yield (%)	MP (°C)	Molecular Formula	Elemental Analysis				
				C Cal/found	H Cal/found	Cl Cal/found	N Cal/found	O Cal/found
1	80	80-82	$C_{15}H_{20}ClN_3$	64.85/64.84	7.26/7.22	12.76/12.78	15.13/15.17	-
2	72	79-81	$C_{17}H_{17}Cl_2N_3O$	57.63/57.68	5.97/5.96	20.01/20.06	11.86/11.82	4.52/4.50
3	65	68-80	$C_{18}H_{21}ClN_4O_2$	59.91/59.92	5.87/5.84	9.83/9.82	15.53/15.52	8.87/8.84
4a	68	71-72	$C_{25}H_{24}Cl_2N_4O_2$	62.12/62.13	5.00/5.08	14.67/14.61	11.59/11.52	6.62/6.69
4b	56	75-77	$C_{25}H_{24}ClN_5O_4$	60.79/60.76	4.90/4.96	7.18/7.12	14.18/14.13	12.96/12.90
4c	53	82-84	$C_{26}H_{27}ClN_4O_3$	65.20/65.29	5.68/5.60	7.40/7.42	11.70/11.73	10.02/10.0
5a	54	65-67	$C_{27}H_{26}Cl_2N_4O_4$	59.90/59.97	4.84/4.80	13.10/13.16	10.35/10.30	11.82/11.80
5b	76	180-182	$C_{27}H_{26}ClN_5O_6$	58.75/58.72	4.75/4.72	6.42/6.40	12.69/12.65	17.39/17.33
5c	59	80-82	$C_{28}H_{29}ClN_4O_5$	62.62/62.65	5.44/5.40	6.60/6.57	10.43/10.49	14.90/14.93

Table 2: Antimicrobial Activity of Synthesized Compounds 1, 3, 4a and 5c

S.No.	Conc. (µg/ml)	*E.coli*		*B. substilis*		*A. niger*		*C.albicans*	
		Zone of Inhibition (mm)	% activity compared to the standard	*Zone of Inhibition (mm)*	% activity compared to the standard	*Zone of Inhibition (mm)*	% activity compared to the standard	*Zone of Inhibition (mm)*	% activity compared to the standard
1	400	14	50.00	16	53.33	38	58.46	16	55.17
	200	12	54.55	11	47.82	26	43.33	11	47.82
	100	10	62.50	7	41.17	-	-	8	44.44
3	400	15	51.00	17	54.34	54	59.43	17	56.18
	200	13	56.56	12	48.81	45	44.38	12	48.81
	100	11	60.50	8	44.18	-	-	9	45.44
4a	400	21	66.86	26	83.31	55	82.51	19	63.02
	200	18	67.64	17	74.90	46	72.39	14	57.50
	100	11.6	58.31	12	65.70	-	-	10	51.00
5c	400	19	68.28	21	67.63	39	79.34	24	73.41
	200	17	76.70	14	57.52	27	66.00	17	61.87
	100	10	60.26	10	53.94	-	-	12	56.55
Streptomycin	400	20	72.80	22	71.00	52	82.09	22	80.30
	200	15	79.29	15	61.83	40	77.65	15	70.56
	100	10.5	74.81	11	59.89	-	-	-	-
fluconazole	400	-	-	-	-	66	100	30	100
	200					61	100	24	100
	100					-	-	19	100

Antimicrobial activity

The in vitro antimicrobial activity of compounds **1, 3, 4a and 5c** was performed using the disk diffusion method. Streptomycin for bacteria and fluconazole for fungal were used as standard drugs. The compounds **1, 3, 4a and 5c** were tested for their anti-bacterial and anti-fungal activities by disk-diffusion method using nutrient broth medium [contained (g/l): beef extract 3 g; peptone 5 g; pH 7.0] for bacteria and potato dextrose broth medium [contained (g/l): beef extract 3 g; peptone 5 g; pH 7.0] for fungi .The Gram-positive bacteria and Gram-negative bacteria utilized in this study consisted of *E. coli*, and *B. substilis* for bacterial species and *A.niger* and *C.albicans* for the fungal species. In the disk-diffusion method, sterile paper disks (0.5 mm) impregnated with compound dissolved in dimethylsulfoxide (DMSO) at concentration 100, 200 and 400 µg/ml were used. Then, the paper disks impregnated with the solution of the tested compounds were placed on the surface of the media inoculated with the microorganism. The plates were incubated at 35°C for 24 hrs. After incubation, the growth inhibition zones and activity checked out. The outcome of this study is presented in **table 2**.

The antibacterial activity was evaluated against two pathogenic strains (*E.coli.* and *B.subtilis*). The zone of inhibition and activity index were determined by comparison with the standard drug streptomycin. The outcome of this study is presented in table-II. The antibacterial screening against *E.coli* showed that amongst the compounds 1,3,4a and 5c, the compound 5c displayed highest activity. The compound 1 showed minimum activity amongst all the compound. The remaining compounds 4a and 3 showed only moderate activity. Contrary to this observation, compound 3 showed highest activity amongst all the compounds screened for this activity against *B.subtilis*.

Similarly the antifungal activity was evaluated against two pathogenic strains (*A.niger and C.albicans*). The zone of inhibition and activity index were determined by comparison with the standard drug fluconazole. The outcome of this study is presented in table 2. The antifungal screening against A.niger showed that amongst the compounds 1, 3,4a and 5c the compound 4c displayed highest activity. The compound 1 showed minimum activity amongst the entire compound. The remaining compounds 5c and 3 showed only moderate activity. Contrary to this observation, compound 5c showed highest activity amongst all the compounds screened for this activity against *C.albicans*.

The importance of such work lies in the possibility that the new compound might be a more efficacious drug against bacteria for which a thorough investigation regarding the structure–activity relationship, toxicity and in their biological effects which could be helpful in designing more potent anti-bacterial and fungal agents for therapeutic use.

CONCLUSION

This research involves the synthesis of oxazolidinone derivatives. The antitoxicity, anti-bacterial and antifungal activity of these compounds was examined using culture of bacteria and fungal and results showed that the addition of the oxazolidinone ring on the quinoline molecule framework increased the antitoxicity, anti-bacterial and antifungal activity. Among the entire four compounds oxazolidinone derivative showed better antitoxicity, anti-bacterial and fungal activity than the respective drug streptomycin and fluconazole.

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