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Synthesis of New Coumarin Derivatives as Antibacterial Agents

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Abstract: 3-[(2'-Substituted benzylidene amino thiazol-4'-yl) amino] coumarins **(5a-5d)** and 3-[(2'-Substitutd benzylidine amino oxazole-4'-yl) amino coumarins **(8a-8d)** were prepared by the reaction with compounds **4** and **7** respectively with various substituted aldehydes in the presence of glacial acetic acid. All the synthesized compounds **1-20** have been screened for their antibacterial and antifungal activities and compared with reference drugs ciprofloxacin, gattifloxocin, luconazole.

Key words- Coumarins, thiazole, oxazole, azetidinone, antibacterial and antifungal activities.

Introduction

Coumarin derivatives are important source of heterocyclic compounds of pharmocological interest, as they shown a wide spectrum of biological activity viz antibacterial[1,2] antifungal[3,4], herbicidal[5] and antitumour[6] activities. Furthermore it has been reported by different scientists that coumarin derivatives incorporating thiazole[7], azetidinone [8] and oxazole[9] ring were also found to possess interesting antibacterial and antifngal activities. In the light of these observation several new coumarin derivatives possessing thiazole, oxazole and □-lactum ring will be synthesized with the hope to possess better antibacterial agents. Compound 9c 3-[2{4-methoxy phenyl-3"-chloro 4"-oxoazetidin-1"-yl) oxazol-4'-yl} amino] coumarin was found to be most potent antibacterial compound against E. coli and K. pneumoniae and compound 9d was found to be most potent antifungal agents against C. albicans. The structure of all the compound were established on the bases of IR and ^{1}H NMR.

Material & Methods

The melting points of the compounds were determined in open glass capillaries with the help of thermonic melting point apparatus and are uncorrected. The homogeneity of all the newly synthesized compounds was routinely checked by thin layer chromatography (TLC) on silica gel G plates. The IR spectra were recorded on a Beckman Acuulab-10. Spectrometer (ν max in cm^{-1}) and the ^{1}H NMR spectra were recorded by Brucker DPX-300MHz using $CDCl_3$ as solvent.

Synthesis of 3-Acetylamino-coumarin (1)

It was prepared according to the method by Tripathy and Mukerjee[10]. To the suspension of aceturic acid (0.005 mol) in dry benzene (25 mL) containing triethylamine (0.0125 mol), benzenesulphonyl chloride (0.005 mol) was added and the mixture was shaken at room temperature untill the aceturic acid crystal disappeared and triethylamine salt separated out which were filtered and washed with benzene (10 mL). To the benzene filtrate salicyladehyde (0.005 mol) was added. The mixture refluxed for 2 h. After refluxing the solution was concentrated upto dryness and the residue obtained was treated with a groups ethanol and filtered. The separated solid was recrytallized from aqueous ethanol. Physical and analytical data are given in table-1.

Table-I Physical and analytical data of compounds 1 to 20

Comp. No.	R'	M.P 0°C	Yield %	Recrystalization solvent	Molecular Formula	Element Analysis % C		% H		% N	
						Calcd	Found	Calcd	Found	Calcd	Found
1.	–	205	54	ethanol	$C_{11}H_9NO_3$						
2.	-	130	44	ethanol	$C_9H_7NO_2$						
3.	-	145	35	ethanol	$C_{11}H_8NO_3cl$	55.57	55.68	3.36	3.42	5.89	6.01
4.	-	151	65	Methanol water	$C_{12}H_9N_3O_2S$	55.59	55.87	3.47	3.09	16.21	16.52
5a	H	159	40	Methanol	$C_{19}H_{13}O_2N_3S$	65.71	65.83	3.75	3.89	12.10	12.37
5b	p-OH & m-OCH_3	158	35	Ethanol water	$C_{20}H_{15}O_4N_3S$	61.07	61.41	3.82	3.52	10.68	10.78
5c	p.OCH_3	126	50	D.M.F.	$C_{20}H_{15}O_3N_3S$	63.66	63.78	3.98	3.78	11.14	11.32
5d	O-OH	162	45	Benzene	$C_{19}H_{13}O_3N_3S$	62.81	62.77	3.58	3.42	11.57	11.29
6a	H	167	50	Methanol-water	$C_{21}H_{14}O_3N_3Scl$	59.50	59.28	3.30	3.48	9.92	9.64
6b	p-OH & m-OCH3	126	15	Acetone	$C_{22}H_{16}O_5N_3Scl$	56.23	56.56	3.41	3.31	8.95	8.71
6c	p-OCH3	110	20	DMF	$C_{22}H_{16}O_4N_3Scl$	58.21	58.43	3.53	3.33	9.26	9.18
6d	O-OH	98	25	Ethanol-water	$C_{21}H_{14}O_4N_3Scl$	57.34	57.18	3.18	3.43	9.56	9.78
8a	H	160	60	Ethanol	$C_{19}H_{13}O_3N_3$	68.88	68.64	3.93	3.99	12.68	12.45
8b	p-OB & m-OCH_3	155	25	DMF	$C_{20}H_{15}O_5N_3$	63.48	63.24	3.97	3.72	11.14	11.25
8c	p-OCH_3	192	40	Methanol	$C_{20}H_{15}O_4N_3$	66.48	66.18	4.15	4.30	11.63	11.50
8d	O-OH	142	20	Benzene	$C_{19}H_{13}O_4N_3$	65.70	65.54	3.74	3.52	12.10	12.02
9a	H	172	50	Ethanol-water	$C_{21}H_{14}O_4N_3Cl$	61.84	61.76	3.43	3.57	10.31	10.48
9b	p-OH & m-OCH_3	160	50	Benzene	$C_{22}H_{16}O_6N_3Cl$	58.21	58.35	3.53	3.45	9.26	9.18
9e	p-OCH_3	142	35	DMF	$C_{22}H_{16}O_6N_3Cl$	60.34	60.44	6.35	3.60	9.60	9.78
9d	O-OH	125	30	$CHCl_3$	$C_{21}H_{14}O_5N_3Cl$	59.50	59.43	3.30	3.15	9.92	9.82

Synthesis of 3-Amino coumarin (2)

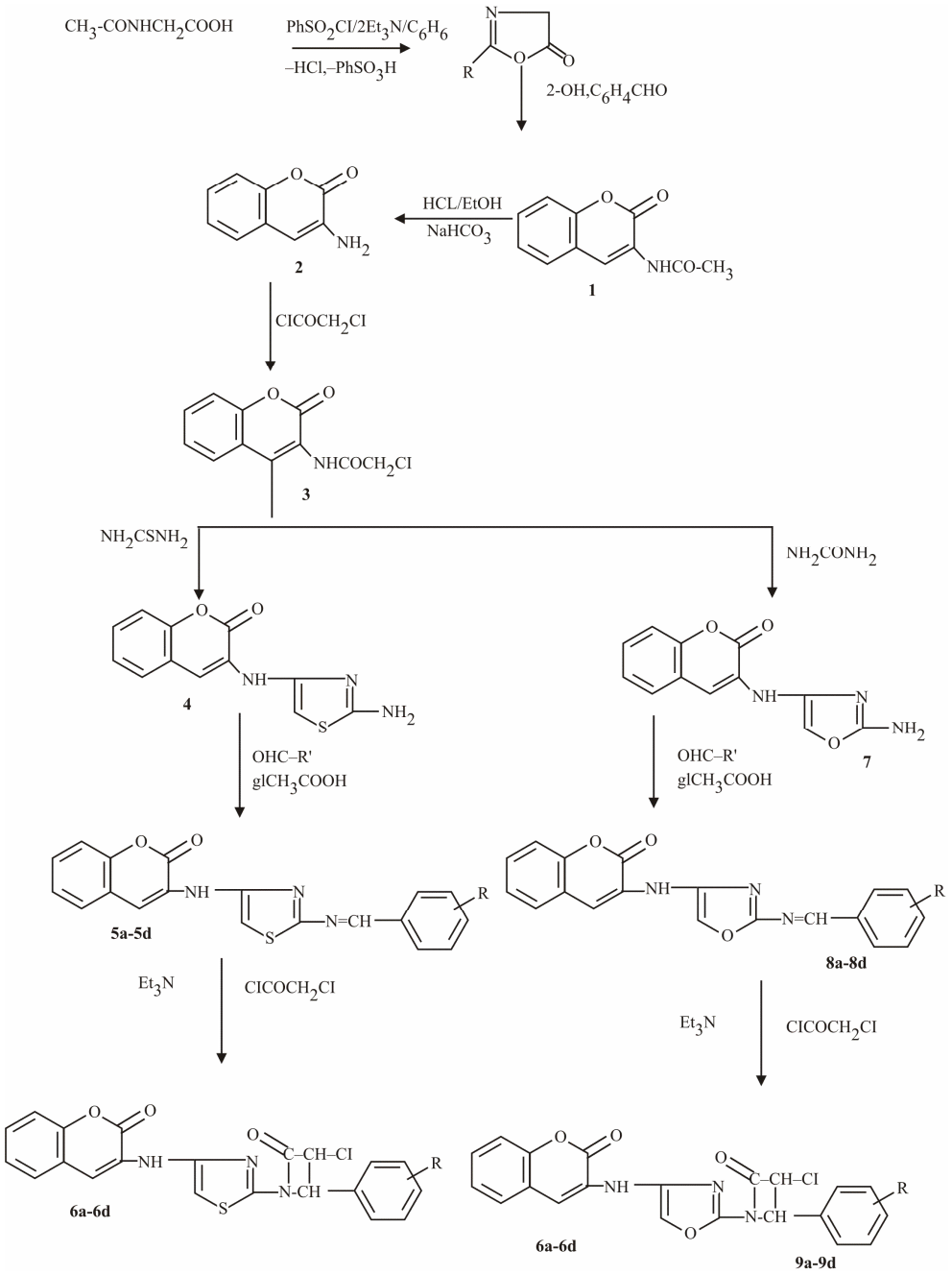
It was prepared according to Tripathy and Mukerjee acetyl amino coumarin **1** was treated with ethanol /con. HCl / 50 ml) 25 mL per g of aceturic acid) and the mixture refluxed for 15 min. The solution was concentrated on a steam bath, diluted with water and to the clear solution $NaHCO_3$ added until it was alkaline. The resultant solid which was filtered, washed with water and recrystallised from ethanol to give compound **2** physical analytical and spectral data are given in table -1, 2 respectively.

3-Chloro acetyl amino Coumarin (3)

To a methanolic solution of compound **2** (0.01 mol), chloroacetyl chloride (0.02 mol) was added. The reaction mixture was kept at room temp. for 6 h, refluxed, distilled off and then poured into crushed ice. Filtered and finally recrystallized from ethanol water to give compound **3.** Physical, analytical and spectral data are given in table 1 and 2 respectively.

3[-(2'-Amino thiazole-4'-yl) amino]-coumarin (4)

To a methanolic solution of compound **3** (0.01 mol) thiourea (0.01 mol) was added. The reaction mixture was refluxed for 12 h distelled, poured on to crushed ice and resulant solid was recrystallised with methanol water physical, analytical and spectral data are given in table 1 and 2 respectively.



Scheme I

General procedure for Synthesis of 3- [(2'-Substituted benzylidene amino thiazol-4'-yl) amino] coumarins (5a-5d)

To the solution of compound (4) (0.01 mol) in methanol (50 mL), substituted benzaldehyde (0.01 mol) was added and refluxed for 12 h. After refluxing the reaction mixture was concentrated to half of its volume and poured onto crused ice. The solution was distilled off and the residue thus obtained was washed with water and finally recrystallised from methanol to give compounds **5a-5d**. The physical , analitical and spectral data are given in table 1 and 2 respectively.

General procedure for Synthesis of 3-[2'-{(2"-Substituted phenyl-3"-chloro-4"-oxoazitidin-1"yl) thiazol-4'-yl} amino] coumarins (6a-6d)

To a methanolic solution (50 mL) of compound **5a-5d** (0.01 mol) chloro acetyl chloride (0.01 mol) and few drops of triethylamine at 0-5ºc was added. Then reflux the solution for 1h. The reaction mixture was poured onto crushed ice. The solid thus obtained were washed with water, filtered and recrystallized with methanol water to furnished compounds **6a-6d.** Physical, analytical and spectral data are given in table 1 and 2 respectively.

Table-2 spectral date of compounds 1-20

Comp. No.	$[M]^+$ m/z	IR (KBr) V max in Cm^{-1}	^{1}H-NMR (CDCl3+ $DMSOd_6$) δ in ppm
3.	237	620 (C-Cl), 1134 (C-O-C) 1510 (C⋯⋯C of aromatic ring), 1650 (C=O), 1731 (C=O), 3270 (N-H)	5.56 (s,2H, $COCH_2$), 6.25 (s, 1H, C-4H of coumarin), 7.25-7.70 (m, 4H, ArH), 8.90 (bs, 1H, NH)
4.	259	675 (C-S-C), 1132 (C-O-C), 1510 (C⋯⋯C of aromatic ring), 1630 (C-N), 1680 (C=O), 3225 (N=H), 3412 (NH_2)	4.10 (bs, IH, NH), 5.10 (S, IH, CH-S), 5.70 (bs, 2H, NH_2), 6.32 (s, 1H, C-4H of coumarin ring), 7.22-7.65 (m, 4H, ArH)
5a	347	676 (C-S-C), 1134 (C-O-C, 1462 (C-N), 1511 (C⋯⋯C of aromatic ring), 1631 (C=N), 1680 (C=O), 3222 (N-H).	4.15 (bs, IH, NH), 5.12 (s, IH, CH-S), 6.3 (s, IH, C-4H of coumarin ring) 6.92-7.78 (m, 7H, ArH), 8.62 (S, 1H, N= CH. Ar)
5b	393	676 (C-S-C), 1134 (C-O-C), 1462 (C-N), 1512 (C⋯⋯C of aromatic ring), 1633 (C=N), 1682 (C=O), 3225 (N-H), 3550 (OH), 1225 (O-CH_3)	4.16 (bs, 1H, NH), 5.11 (S, 1H, CH-S), 6.8 (s, 1H, C-4H of coumarin ring), 6.95-7.78 (m, 7H, ArH), 8.68 (s, IH, N=CH-Ar), 11.29 (s, 1H, OH), 3.41 (s,3H, OCH_3)
5c	377	674 (C-S-C), 1136 (C-O-C), 1464 (C-N), 1515 (C⋯⋯C of aromatic ring), 1634 (C=N), 1680 (C=O), 3226 (N-H), 1226 (O-CH_3)	4.18 (bs, 1H, NH), 5.14 (s,IH,CH-S), 6.8 (s, IH, C-4H of coumarin ring), 6.97-7.79 (m, 8H, ArH), 8.69 (s,1H, N=CH-Ar), 3.42 (S,3H, OCH_3)
5d	363	678 (C-S-C), 1137 (C-O-C), 1468 (C-N), 1515 (C⋯⋯C of aromatic ring), 1635 (C=N) 1684 (C=O), 3228 (N-H), 3552 (OH)	4.18 (bs, 1H, NH), 5.13 (s,IH, CH-S), 6.8 (s, 1H, C-4H of coumarin ring), 6.96-7.79 (m, 8H, ArH), 8-69 (s, 1H, N=CH-Ar), 11.30 (s, 1H, OH)
6a	423	674 (C-S-C), 760 (C-Cl), 1132 (C-O-C), 1462 (C-N), 1511 (C⋯⋯C of aromatic ring), 1632 (C=N), 1690 (C=O), 1760 (C=O) of β-lactum ring, 3225 (NH)	4.16 (bs, 1H, NH), 4.65 (d, IH, CH-CI), 5.05 (S, 1H, CH-S), 6.40-6.48 (d, 1H,N-CH-Ar), 6.63 (S,1H, C-4H of coumarin ring), 6.90-7.75 (m,9H, ArH)
6b	469	675 (C-S-C), 761 (C-Cl), 1134 (C-O-C), 1463 (C-N), 1512 (C⋯⋯C of aromatic ring), 1634 (C=N), 1691 (C=O), 1762 (C=O) of β lactum ring, 3226 (NH), 3550 (OH), 1225 (O-CH_3)	4.18 (bs, 1H, NH), 4.66-4.83 (d, 1H, CH-cl), 5.06 (s, IH, CH-S, 6.41-6.47 (d, 1H, N-CH-Ar), 6.68 (S,IH, C-4H of coumarin ring), 6.91-7.76 (m, 7H, Ar H), 11.32 (s, 1H, OH), 3.43 (s, 3H, OCH_3)
6c	453	676 (C-S-C), 764 (C-Cl), 1135 (C-O-C), 1464 (C-N), 1514 (C⋯⋯C of aromatic ring), 1634 (C=N), 1692 (C=O), 1767 (C=O) of β-lactum ring, 3225 (NH), 1226 (O-CH_3)	4.18 (bs, 1H,NH) 4.65-4.85 (d, 1H, CH-C), 5.06 (s, 1H, CH-S), 6.42-6.48 (d,1H, N-CH-Ar), 6.69 (s, 1H, C-4H of coumarin ring), 6.92-7.778 (m, 8H, ArH), 3.45 (S, 3H, OCH_3)
6d	439	677 (C-S-C), 761 (C-Cl), 1135 (C-O-C), 1464 (C-N), 1514 (C⋯⋯C of aromatic ring), 1635 (C=N), 1692 (C=O), 1762 (C=O) of β-lactum ring 1325 (NH), 3552 (OH)	4.19 (bs, 1H, NH), 4.66-4.84 (d, 1H, CH-cl), 5.05 (S,1H, CH-S), 6.43-6.47 (d, 1H, N-CH-Ar), 6.68 (s, 1H, C-4H of Coumarin ring), 6.93-7.77 (m, 8H, ArH), 11.34 (s, 1H,OH)
8a	331	1070 (C-O-C), 1131 (C-O-C), 1459 (C-N), 1510 (C⋯⋯C of aromatic ring), 1630 (C=N), 1682 (C=O), 3224 (NH),	4.12 (bs, 1H, NH), 5.30 (S,1H, CH-O), 6.41 (s,1H, C-4H of coumaring ring), 6.90-7.76 (m, 9H, ArH), 8.60 (s, 1H, N-CH-Ar)

8b	377	1072 (C-O-C), 1132 (C-O-C), 1458 (C-N), 1512 (C⋯⋯C of aromatic ring), 1632 (NH), 1684 (C=O), 3225 (NH), 3550 (OH), 1225 (O-CH_3)	4.14 (bs, 1H, NH), 5.32 (s,1H, CH-O), 6.42 (s,1H, (-4H of coumaring ring), 6.91-7.78 (m, 7H, ArH), .62 (s, 1H, N=CH-Ar), 11.32 (s, 1H, OH), 3.43 (s, 3 H, OCH_3
8c	361	1071 (C-O-C), 1133 (C-O-C), 1457 (C-N), 1514 (C⋯⋯C of aromatic ring), 1634 (C=N), 1683 (C=O), 3225 (NH), 1226 (O-CH_3)	4.13 (bs, 1H, NH), 5.33 (s,1H, CH-O), 6.42 (s,1H, (-4H of coumaring ring), 6.91-7.78 (m, 7H, ArH), .62 (s, IH, N=CH-Ar), 11.32 (s, 1H, OH), 3.43 (S, 3 H, OCH_3
8d	347	1073 (C-O-C), 1134 (C-O-C), 1458 (C-N), 1513 (C⋯⋯C of aromatic ring), 1633 (C=N), 1682 (C=O), 3225 (NH), 3552 (OH)	4.14 (bs, 1H, NH), 5.34 (s, iH, CH-O), 6.43 (s, 1H, C-4H of coumarin ring). 6.94-7.78 (m, 8H, ArH), 8.61 (s, IH, N= CH-Ar), 11.34 (s, IH,OH)
9a	407	761 (C-Cl), 1132 (C-O-C), 1463 (C-N), 1510 (C⋯⋯C of aromatic ring), 1632 (C=N), 1690 (C=O), 1762 (C=O of β-lactum ring), 3223 (NH)	4.15 (bs, IH, NH), 4.60-4.81 (d, IH, CH-Cl), 5.30 (s, IH, CH-O), 6.50- 6.60 (d,1H, N-CH-Ar), 6.45 (s, IH, C-4H of coumaring ring), 6.88-7.78 (m, 9H, ArH)
9b	453	762 (C-Cl), 1134 (C-O-C), 1464 (C-N), 1512 (C⋯⋯C of aromatic ring), 1634 (C=N), 1692 (C=O), 1762 (C=O of β-lactum ring), 3223 (NH), 3550 (OH) 1225 (O-CH_3)	4.15 (bs, IH, NH), 4.62-4.84 (d, IH, CH-Cl), 5.32 (s, 1H, CH-O), 6.52- 6.62 (d,1H, N-CH-Ar), 6.46 (s, 1H, C-4H of coumaring ring), 6.89-7.78 (m, 1H, ArH), 11.32 (s, 1H, OH), 3.43 (s, 3H, OCH_3)
9c	437	764 (C-Cl), 1135 (C-O-C), 1465 (C-N), 1514 (C⋯⋯C of aromatic ring), 1635 (C=N), 1693 (C=O), 1763 (C=O of β-lactum ring), 3223 (NH), 1225 (O-CH_3)	4.18 (bs, 1H, NH), 4.63-4.82 (d, 1H, CH-Cl), 5.34 (s, 1H, CH-O), 6.53- 6.63 (d,1H, N-CH-Ar), 6.48 (s, 1H, C-4H of coumaring ring), 6.88-7.78 (m, 8H, ArH), 3.44 (s, 3H, OCH_3)
9d	423	765 (C-Cl), 1136 (C-O-C), 1467 (C-N), 1515 (C⋯⋯C of aromatic ring), 1636 (C=N), 1692 (C=O), 1764 (C=O of β-lactum ring), 3223 (NH), 3552 (OH).	4.17 (bs, IH, NH), 4.64-4.84 (d, 1H, CH-Cl), 5.33 (s, 1H, CH-O), 6.54- 6.64 (d,1H, N-CH-Ar), 6.49 (s, 1H, C-4H of coumarin ring), 6.89-7.77 (m, 8H, ArH), 11.34 (s, 1H, OH).

Synthesis of 3- [(2'-Amino oxazol-4'-yl) amino] coumarin (7)

To a methanolic solution of compound **3** (0.01 mol), Urea (0.01 mol) was added. The reaction mixture was refluxed at 9h distilled, poured into ice cold water, filtered and finally recrystallized from methanol water.

eneral procedure for Synthesis of 3-[(2'-Substituted benzylidene amino oxazol-4'-yl) amino] coumarins 8a-8d :

A solution of compound **7** (0.01 mol) in methanl, substituted benzeldehyde (0.01 mol) was added and refluxed for 12 h. After refluxing the reaction mixture was concentrated to half of its volume and poured on to crushed ice. The solution was distilled off and the residue thus obtained and washed. several time with water and finally recrystallized from ethanol to yielded compounds **8a-8d.** Physical, analytical and spectral data given in table 1 and 2 respectively.

General procedure for Synthesis of 3-[2'-{(2"-Substituted phenyl-3"-chloro-4"-oxozetidin 1"-yl) oxazol-4'-yl} amino] coumarin (9a-9d)

To a methanolic solution of compound **8a** (0.01 mol) add chloro acetyl chloride (0.01 mol) and few drops of triethylamine at 0-5ºC. The reaction mixture was reflux for 6 h. Poured into ice cold water. The resultant solid thus obtained was washed with water filtered and recrystallized with ethanol water to given compounds **9a-9d.** Physical, analytical spectral data are given in table 1 and 2 respectively.

Table-3

Compound No.	R	Bacterial Growth inhibition (diameter)				Fungal growth in hibition (diameter)	
		S. Aureus 209 P	E.Coli ESS2231	P. Vulgaris	K. Pneumonial	C. albicans	C. albicams ATCC 10231
4	-	6 mm	7 mm	8 mm	6 mm	-	-
5a	H	8 m	5	6	-	-	-
5b	P-OH & m-OCH_3	6	-	5	8	-	-
5c	p-OCH_3	12	10	14	-	-	-
5d	o-OH	-	10	8	7	10	12
6a	H	-	-	-	-	-	-
6b	P-OH & M-OCH_3	10	-	14	12	-	-
6c	P-OCH_3	15	18	15	16	-	-
6d	O-OH	8	10	9	6	12	16
7	-	-	-	-	-	-	-
8a	H	-	-	-	-	-	-
8b	p-OH & m-OCH_3	18	17	12	14	10	12
8c	p-OCH_3	19	22	16	20	8	6
8d	0-OH	14	-	12	18	16	18
9a	H	15	18	-	20	12	16
9b	p-OH & m-OCH_3	20	-	26	18	18	16
9c	p-OCH_3	28	30	21	22	-	-
9d	o-OH	-	9	-	-	30	-
Ciprofloxacin		20	22	20	20	-	-
Gattifloxacin		25	22	20	20	-	-
Fluconazole		-	-	-	-	29	25

Pharmacological Evaluation

All the synthesized compounds have been evaluated for antibacterial and antifungal activity. For antibacterial screening various bacteria, staphylococcus aureus 209 P, E. Coli ESS 2231, proteus vulgaris, K. Pneumoniae were used. Antifungal activity were performed against candida albicans, candida albicans ATCC 10231. The screening results were compared with gattifloxacin and ciprofloxacin for antibacterial and fluconazole for antifungal activities respectively and propylene glycol treated group served as control. All the newly synthesized compounds were also screened for their approximate lethal dose (ALD_{50}).

Cup-plate Method (Chuinckshank[11] et al 1975)

(a) Antibacterial activity

Nutrient agar was poured onto the sterilized Petri dishes (20-25 mL. each Petri dish). The poured material was allowed to set (1-1.5 h) and thereafter the "CUPS" (10 mm diameter) was made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. In to these cups the test compound solution was added with the help of sterile syringe. The plates were incubated at 37ºC for 48 h and the result were noted. A solvent control (10% DMSO in methanol) was also run to not the activity of the blank (Solvent). The above said standard drugs were also screened under similar conditions for comparison.

(b) Anti fungal activity :

anti fungal activity was also done by the method of Chuinckshonk et al , 1975 using Fluconazole as standard drug.

Approximate lethal dose (ALD_{50}): The LD_{50} was determined in albino rats weighing 100-120 gm of either sex by the method of Smith[12]. The test compounds were administered by i.p. rout in one group and the same volume of propylene glycol in another group of animals consisting six rats in graded doses. The animals were allowed to take food and water adlibidum. After 24 h of drug administration percent mortality in each group was observed. From the data obtained ALD_{50} was calculated.

Results and Discussion

Various substituted derivatives of coumarins were synthesized and screened for their antibacterial as well as antifungal activity. Screening results of these compounds are given in table- IV. Compound **4** exhibited very less anti bacterial activity and was devoid of anti fungal activity. Benzylidene substituted coumarins **5a, 5b and 5d** did not showed any remarkable bacterial activity whereas, compound **5c** (Which was substituted with 4-OCH_3 group) elicited good antibacterial activity than **5a-5b** and **5d**, The compound **5a, 5c** and **5b** did not exhibited antifungal activity. While **5d** showed good antifungal activity. Cyclization of these compounds by chloroacetyl chloride in presence of triethylamine yielded corresponding azetidinones **6a-6d.** Compound **6c** was found to possess moderate bactericidal property against all the selected strain and was devoid of antifungal activity. Furthermore compound **6d** showed less antibacterial property against all the bacterial strains and this compound showed good antifungal activity against C. albicans and C. Albicans ATCC. The compound **6a** did not exhibited antibacterial as well as antifungal activity . Among **8a**, **8b, 8c** and **8d**, compound **8c** which was substituted with methoxy gp at position 4th of phenyl ring showed potent anti bacterial activity (19mm, 22 mm, 16 mm and 20 mm) than compound **8a, 8b** and **8d.** Compound **8d** elicited moderate antifungal activity and was associated with mild to moderate antibacterial activity. Oxazolyl benzylidene coumarins **8a-8d** cyclized by means of chloroacetyl chloride in presence of triethyl amine to furnish corresponding oxazolylazetidinonyl coumarins **9a-9d,** In these compounds, compound **9c** showed potent antibacterial activity while the compound **9d** exhibited most potent antifungal activity. Compound **9a** showed 15, 18 and 20 mm zone of inhibition against S. aureus, E. coli ESS 2231 and K. pneumonial respectively. While compound **9 b** showed the 20, 26 and 18 mm zone of inhibition. The result suggest compound **9 a** was found to possess good antibacterial activity. On the other hand compound **9b** exhibited better antibacterial and antifungal response as compare to **9a.**

Discussion

In general, cyclized compounds showed better activity than their parent compounds. 4-OCH_3 Substituted azetidinone moiety **9c** is scems to be beneficial bactericidal compound against all the bacterial strain in comparison to clinically used drug as gattifloxacin, Ciprofloxacin. 2-Hydroxy substitution is also found to be beneficial for fungicidal activity against C. albicans ATCC 10231.

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