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Research Article

ANTIMICROBIAL STUDY (*INVITRO*) OF SOME ARYL 1, 4–DIHYDRO PYRIDINE DERIVATIVES

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ABSTRACT

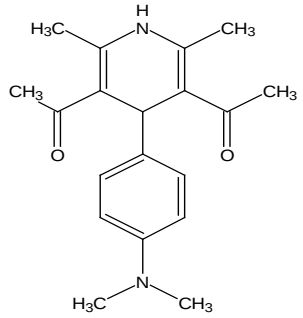
A novel series of aryl 1, 4-dihydro pyridine derivatives were synthesized and investigated for their antibacterial activity against Gram positive and Gram negative bacteria using antibiotic diffusion method. The recorded data of zone of inhibition showed significant broad activity when compared with standard. The sensitivity of the Gram positive bacteria to the synthesized compounds was higher than that of Gram negative bacteria. The synthesized compounds were also found to have an inhibitory effect against the tested pathogenic fungi using Broth dilution Susceptibility test.

Keywords: 1, 4-dihydropyridine derivative, Antibacterial activity, Antifungal activity, Zone of inhibition.

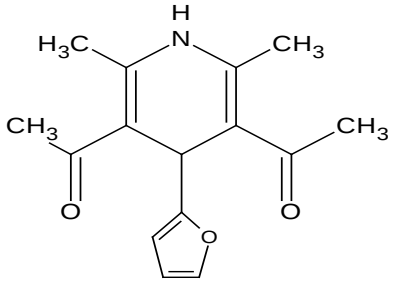
INTRODUCTION

Infectious diseases caused by bacteria affect millions of people and are leading to death worldwide. Treatment of infectious diseases still remains an important and challenging problem because of a combination of factors including emerging and increasing number of multidrug resistant microbial pathogens. Fungal infections are reported to cause lots of morbidity and mortality despite recent advances in antifungal chemotherapeutic regimen[1]. Recently much effort has been devoted to developing more efficient methods for the synthesis of 1,4-dihydropyridines. Some derivatives have been reported as antimicrobial and antimycobacterial agents. Five novel 1, 4- dihydro pyridine derivatives (CR1-CR5) were synthesized and characterized. All the synthesized compounds bearing1,4- dihydro pyridine nucleus, were reported to possess a number of interesting biological activities such as anti hypertensive, antituberculosis, bronchodilating, hepatoprotective, antitumor, antimutagenic, geroprotective, neuroprotective and platelet anti-aggregation, antidiabetic and anti inflammatory activity.

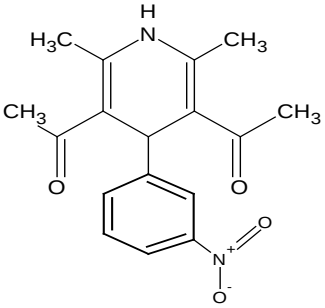
Moreover a number of DHP's acts as calcium antagonists. Recent studies have revealed that 1, 4-dihydropyridines also exhibit other treatment of Alzheimer's disease and as a chemo sensitizer in tumor therapy.[2-6] The synthesis of these compounds involves Hantzsch reaction. An economical, solvent free, very efficient, eco-friendly synthesis of 1, 4-dihydropyridines which can be a viable alternative to their conventional synthesis has been developed. The experimental data and its spectral data of the said derivatives had already been sent for publication (under review). All the synthesized compounds were screened for antibacterial and antifungal activity. Furthermore, investigation of the relationship between the antimicrobial effect and the structure of 1, 4-dihydro pyridine derivatives were studied. The structures of the synthesized compounds are as follows:



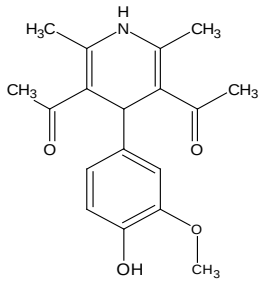
CR1



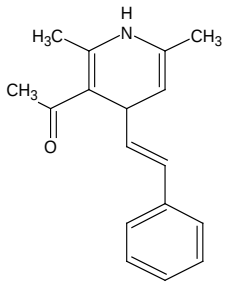
CR2



CR3



CR4



CR5

Where,

CR1-1, 1'-{4-[4-(dimethylamino) phenyl]-2,6-dimethyl-1,4-dihydropyridine-3,5- diyl}diethanone.
CR2-1, 1'-[4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl] diethanone**.**
CR3-1, 1'-[2, 6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-diyl]diethanone - methane (1:1).
CR4-1, 1'-[4-(4-hydroxy-3-methoxyphenyl)-2, 6-dimethyl-1, 4-dihydropyridine-3,5- diyl]diethanone.
CR5-1, 1'-{2, 6-dimethyl-4-[(E)-2-phenylethenyl]-1, 4-dihydropyridine-3, 5-diyl} diethanone.

MATERIALS AND METHODS

Antibacterial Activity [7,8,9]

The synthesized compounds (CR1-CR5) were evaluated for their antibacterial activity. Various organisms used for *invitro* study include Gram negative organisms such as *Escherichia coli, Klebsiella spp, Pseudomonas aeruginosa*, *Salmonella paratyphi A, Salmonella paratyphi B*, Gram positive organisms include *Enterococci, Staphylococcus aureus*, and coagulase-negative *staphylococci*. MIC values of the test compounds were determined by dilution technique. The organism was sub cultured on Muller Hinton Agar medium. DMSO was used as negative control and ciprofloxacin ((5µg/ml) as standard. Four different concentrations (133.33µg/mL)/ml, 200 µg/mL, 333.33 µg/mL, and 400 µg/mL) were used to determine the MIC. Zone of inhibition of the individual compounds were studied by antibiotic diffusion method. Diameters of the zone of inhibition in mm for the test compounds at 400 µg/ml /ml were measured and compared with that produced by the standard drug. The results of the study are presented in Table 1 and Table 2.

Antifungal Activity[10]

The antifungal was determined by performing Broth dilution susceptibility test. The antifungal activities of tested compounds against the pathogenic fungi *Aspergillus flavous, Aspergillus niger and Rhizopus* at 16, 8, 4, 2, 1, 0.5, 0. 25, 0.125, 0.0625, and 0.0313µg/mL concentrations were studied. The fungi were sub cultured in RPMI 1640 agar medium. The susceptibility of the fungi was done by comparing the growth of the pathogenic control of the test compound with the fluconazole standard. The fungal study related data are given in table 3.

Table 1: Antimicrobial activity

S. No.	Name of the organism	Minimum inhibitory concentration(µg/mL)																			
		CR1				CR2				CR3				CR4				CR5			
		133.33	200.00	333.33	400.00	133.33	200.00	333.33	400.00	133.33	200.00	333.33	400.00	133.33	200.00	333.33	400.00	133.33	200.00	333.33	400.00
1	*Enterococci*	+	+	+	-	+	+	+	-	+	+	-	-	+	+	+	-	+	+	-	-
2	*coagulase- negative staphylococci*	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	-
3	*Staphylococcus aureus*	+	+	+	-	+	-	-	-	+	+	+	-	+	+	+	-	+	+	+	-
4	*Escherichia coli*	+	+	+	-	+	-	-	-	+	+	-	-	+	+	+	-	+	+	-	-
5	*Klebsiellaspp*	+	+	_	-	+	+	-	-	+	+	-	-	+	+	+	-	+	+	+	-
6	*Pseudomonasaeruginasa*	+	+	-	-	+	+	+	-	+	+	-	-	+	+	+	-	+	+	-	-
7	*Salmonellaparatyphi A*	+	+	+	-	+	+	-	-	+	+	-	-	+	+	+	-	+	+	-	-
8	*Salmonellaparatyphi B*	+	+	-	-	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	-

Note: (+) indicate growth, (-) indicate no growth

Table 2: Zone of inhibition of 1, 4- dihydropyridine derivatives

S.no	Name of the organism	Zone of inhibition in mm					
		ciprofloxacin	CR1	CR2	CR3	CR4	CR5
1	*Enterococci*	30	23	24	25	20	26
2	*coagulase –negative staphylococci*	30	22	21	22	21	22
3	*Staphylococcus aureus*	20	17	10	10	20	23
4	*Escherichia coli*	30	15	14	15	16	16
5	*Klebsiellaspp*	30	17	20	21	22	24
6	*Pseudomonasaeruginasa*	29	24	19	19	21	17
7	*Salmonellaparatyphi A*	36	26	20	23	22	23
8	*Salmonella paratyphi B*	40	29	20	21	21	24

Table 3: Antifungal Activity Report

S. No.	Compound Name	Name of the organism	Compound Concentration. (In well at 1:100(µg/ml)				
			16	8	4	2	1
01	CR1	*Aspergillusniger*	+	+	+	+	+
		Aspergillusflavus	+	+	+	+	+
		Rhizopus	+	+	+	+	+
02	CR2	*Aspergillusniger*	+	+	+	+	+
		Aspergillusflavus	+	+	+	+	+
		Rhizopus	+	+	+	+	+
03	CR3	*Aspergillusniger*	+	+	+	+	+
		Aspergillusflavus	+	+	+	+	+
		Rhizopus	+	+	+	+	+
04	CR4	*Aspergillusniger*	+	+	+	+	+
		Aspergillusflavus	+	+	+	+	+
		Rhizopus	+	+	+	+	+
05	CR5	*Aspergillusniger*	-	-	+	+	+
		Aspergillusflavus	-	-	-	-	-
		Rhizopus	+	+	+	+	+

NOTE: (+) indicates growth; (-) indicates no growth.

RESULTS AND DISCUSSION

The synthesized compounds were screened for their antibacterial activity by antibiotic diffusion technique. The comparative study of the zones of inhibition indicated that all the compounds had antibacterial activity. Compounds CR1 was found to be very effective against *Salmonella paratyphi A and B and Klebsilla*. Compound CR2 was found to be more potent against *Salmonella paratyphi B,Pseudomonas aeruginosa.* Compound CR3 found to be very sensitive against *Klebsiella*. Compound CR4 and CR5 was found to be more effective against *Klebsiella,* Coagulase negative *Staphylococci*. All the synthesized compounds were less active against *Escherichia coli.* The *in vitro* antifungal studies of synthesized drug compounds (CR1-CR5) were compared with reference drug fluconazole against various pathogens like *Aspergillus niger, Aspergillus flavus and Rhizopus*. The fungal growth was measured after 24 h incubation at 37˚C. The fungal susceptibility test was done by comparing the growth of pathogenic control and the test compound containing the said cultures. The compound CR5(vinyl substitution in aromatic ring) had activity against *Aspergillus flavous* and *Aspergillus niger*. The compound (CR1-CR4) had no activity against *Aspergillus niger*, *Aspergillus flavous and Rhizopus*. However, the antifungal spectrum of the synthesized compounds were not as effective as that of the reference drug.

CONCLUSION

A series of aryl 1, 4-dihydro derivatives (CR1-CR5) were synthesized. The synthesized compounds were screened for their antibacterial, antifungal activity. Compounds CR1-CR5 were found to possess higher antibacterial activity against *Salmonella paratyphi A* and *B*. In this study the highest antibacterial activity was observed in CR1 which had p- dimethyl amino group as a substituent at 4th position. Of the synthesized compounds, the compound with vinyl substitution in aromatic ring had activity against *Aspergillus flavus* and *Aspergillus niger*.

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