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A study on antimicrobial activity of 1, 8-naphthyridines containing triazinanones, oxadiazinanones, pyrazolyl and substituted pyrimidines

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ABSTRACT

The effect of substituted 1,8-naphthyridine derivatives has been investigated for their antimicrobial activity. Five bacteria *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Micrococcus luteus*, *Proteus mirabilis* and *Salmonella paratyphi*. The antifungal activity of (IV) and (VI) have been investigated against two fungal species *Fusarium chlamydosporium*, *Macrophomina phaseolina*. Some of the tested compounds were found to be toxic against the bacteria and fungi.

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KEYWORDS

Antimicrobial activity;
1,8-naphthyridines
containing triazinanones;
Oxadiazinanones;
Pyrazolyl;
Substituted pyrimidines.

INTRODUCTION

1,8-naphthyridine compounds have been found to be effective in controlling some of the post harvest fungal diseases. Hide and Hirst^[1], Byrde and Willetts^[2] have reported that these compounds are active against several pathogenic fungi. The 1,8-naphthyridine group of compounds have been proved to be active antibacterial agents^[3-5]. One of the 1,8-naphthyridine compound, nalidixic acid (1-ethyl-3-carboxy-7-methyl-1,8-naphthyridin-4-one) was found to be effective against gram negative bacteria of chronic urinary tract infections^[6]. In addition, a variety of pharmacological activities have also been exhibited by 2,3-disubstituted, 1,8-naphthyridines, for example 2-amino-1,8-naphthyridine-3-carboxamide is well known for its diuretic^[7] property. Further, there has been growing interest in screening the 1,8-naphthyridines for their potent antibacterial and antifungal properties.

A number of 1,8-naphthyridines were prepared as

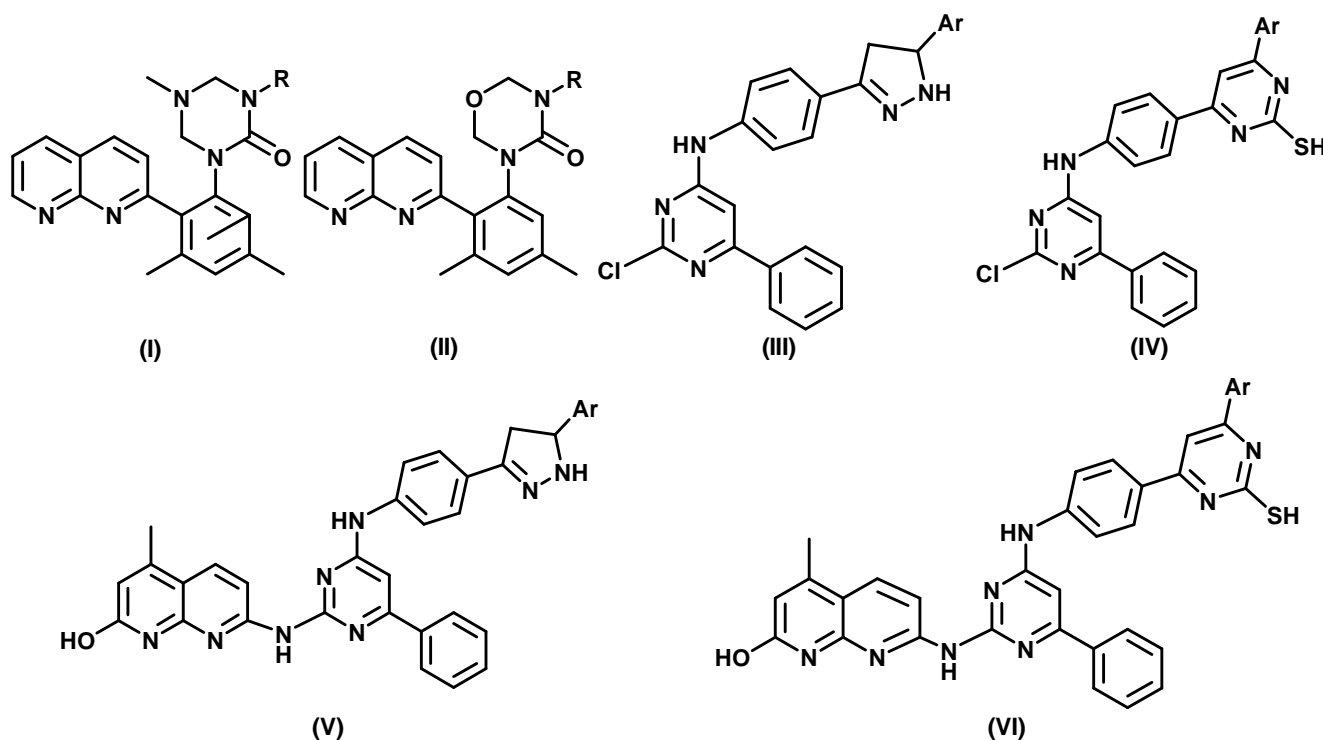
possible bioactive compounds and a very wide range of biological actions are associated with these compound. The activity was found to be enhanced with presence of different substituents. This prompted in the synthesis of many new 1,8-naphthyridine derivatives in the recent past with a view to screen them for their pharmacological activities. A large number of 1,8-naphthyridine derivatives are reported to exhibit antimalarial^[8] and anticancer^[9] activities. Our earlier studies also have shown good antifungal and antibacterial activities^[10-14] of naphthyridines. The present study has been aimed at antimicrobial activity of newly synthesized 1,8-naphthyridine containing triazinanones, oxadiazinanones, pyrazolyl and substituted pyrimidines derivatives. The structures of the compounds are given below.

MATERIAL AND METHODS

The antimicrobial effect of compounds was evaluated using well diffusion method^[15]. All the compounds

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were screened for their *in vitro* antibacterial activity against *Staphylococcus aureus*, *Klebsiella*



pneumoniae, *Micrococcus luteus*, *Proteus mirabilis* and *Salmonella paratyphi*. Tetracycline 100 μ g/ml was dissolved in 5 % aqueous DMF and used for the studies. Antifungal activity of the compounds were done by using Sobourauds agar medium by disk diffusion method. The results were recorded in duplicate. Flucanazole 2.5 mg/L as a standard in DMF solvent. The activity checked was against two fungal species *Fusarium chlamydosporium* and *Macrophomina phaseolina*.

RESULTS AND DISCUSSION

The antibacterial activity of all the substituted 1,8-naphthyridine derivatives were determined against five bacteria strains. Their antibacterial activity are reported in TABLE 1 and TABLE 2. Perusal of the above TABLE 1 reveals that the derivatives having Chloro, Fluoro as substituents were more toxic than simple phenyl compounds towards all five bacteria. Compounds were more growth inhibitory towards *Staph aureus*. (Ib) and (II) were more toxic to the growth of this organism. Derivatives from (Ig) to (IIe) were more toxic towards *Micrococcus luteus*. The compounds synthesized did not show much activity against *Klebsiella pneumoniae*

TABLE 1: Effect of the synthesized compounds I(a-j) and II (a-e) on five bacteria.

Compound No	R	<i>Staphylococcus aureus</i>	<i>Klebsiella pneumoniae</i>	<i>Salmonella paratyphi A</i>	<i>Salmonella paratyphi B</i>	<i>Micrococcus luteus</i>
I a	Phenyl	12	2	-	-	8
I b	Cyclopropyl	19	5	2	5	9
I c	Benzyl	11	2	1	-	7
I d	Cyclohexyl	15	3	1	1	7
I e	Methyl	10	4	3	2	8
I f	Chloro phenyl methyl	10	9	1	5	6
I g	Chloro phenyl cyclohexyl	13	4	3	5	10
I h	Chloro phenyl Benzyl	12	2	1	1	10
I i	Chloro phenyl cyclopropyl	18	4	1	4	10
I j	Chloro phenyl dimethyl	14	2	4	6	10
II a	Chloro phenyl	10	2	2	1	11
II b	Chloro phenyl methyl	14	3	2	6	11
II c	Fluoro phenyl	15	4	4	7	15
II d	Cyclohexyl	13	3	3	4	11
II e	Naphthalenyl	15	4	4	3	10
Tetracycline		25	18	19	16	21

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TABLE 2 : Effect of the synthesized compounds III(a-e), IV (a-e), V(a-e) and VI(a-e) on three bacteria and two fungi.

Compound No	Ar	<i>Staphylococcus Aureus</i>	<i>Klebsiella pneumoniae</i>	<i>Proteus Mirabilis</i>	<i>Fusarium Chlamydosporium</i>	<i>Macrophomina Phaseolina</i>
III a	-H	1	5	-	-	-
IIIb	4-Br	1	8	-	1	1
IIIc	4-Cl	2	10	2	1	-
III d	4-OMe	1	12	1	1	-
III e	2-OH	-	8	1	-	-
IV a	-H	-	7	12	12	14
IV b	4-Br	1	10	14	14	16
IV c	4-Cl	2	15	16	12	15
IV d	2-OMe	1	18	15	15	18
IV e	2-OH	-	14	13	14	12
V a	-H	-	9	-	1	1
V b	4-Br	1	12	-	2	1
V c	4-Cl	1	10	1	6	2
V d	4-OMe	2	13	2	4	2
V e	4-OH	1	12	1	2	-
VI a	-H	13	14	14	10	10
VI b	4-Br	18	16	20	16	17
VI c	4-Cl	18	15	21	14	15
VI d	4-OMe	19	22	18	12	16
VI e	2-OH	22	17	16	10	8
Tetracycline		25	17	22	-----	-----
Flucanazole		-----	-----	-----	18	22

and *Salmonella* group of organisms. Among all compounds, aliphatic compounds were more toxic than aromatic compounds towards all bacteria.

Perusal of the above TABLE 2 reveals that the derivatives having chloro, bromo and methoxy as substituents were found to be more toxic than simple phenyl compound against all three bacteria and two fungi. Compounds of the series (IVa) to (IVe) and (IVa) to (IVc) showed good activities against both the fungi. Rest of the compounds did not show antifungal activity.

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REFERENCES

- [1] G.A.Hide, H.J.Hirst; Rep.Rothansted Exp.stn., **1**, 40 (1970).
- [2] R.J.W.Byrde, H.J.Willetts; The Brown Rot Fungi of Fruit, their Biology and Control, Pergamon Press, Oxford, 171 (1977).
- [3] A.Albert, H.Hampton; J.Chem.Soc., 4237, (1963).
- [4] H.Egawa, T.Miyomoto, A.Minamida, Y.Nishimuray; J.Med.Chem., **27**, 1543 (1984).
- [5] N.Suzuki, Y.Tanaka, Dohmori; Chem.Pharm.Bull., **28**, 235 (1980).
- [6] G.Y.Lesher, E.J.Froctich, M.D.Gruett, J.H.Bailey, R.P.Brondage, J.Med.Chem., **5**, 1063 (1984).
- [7] E.M.Hawes; J.Med.Chem., **20**, 124 (1977).
- [8] G.B.Balier, W.L.Tan; Aust.J.Chem., **37**, 1065 (1984).
- [9] P.L.Ferrarini, C.Moric, G.Biogi, Livio, I.Tonelli; J.Het.Cycl., **24**, 417 (1984).
- [10] K.Mogilaiah, Vijayander Reddy, B.Sreenivasulu; Indian J.Chem., **22B**, 178 (1983).
- [11] Vijayander Reddy, K.Mogilaia, B.Sreenivasulu; J.Indian Chem.Soc., **63**, 443 (1986).
- [12] G.RamaRao, K.Mogilaiah, Rajender Reddy, B.Sreenivasulu; J.Indian Chem.Soc., **64**, 710 (1987).
- [13] M.Thirumala Chary, K.Mogilaiah, G.RamaRao, Sreenivasulu; J.Indian Chem.Soc., **67**, 691 (1990).
- [14] H.Shailaja Rani, K.Mogilaiah, B.Sreenivasulu; Indian J.Het.Cycl.Chem., **5**, 45 (1995).
- [15] C.Perez, M.Paul, P.Bazerque; Acta Biol.Med.Exp., **15**, 113-115 (1990).