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Antibacterial activity of some novel 1,8-naphthyridine containing thiazolidinones, β-lactam and 2,4-dihydroxy compounds

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ABSTRACT

The effect of substituted 1,8-naphthyridine derivatives has been investigated for their antibacterial activity on five different bacteria by well diffusion method. Five bacteria *Staphylococcus aureus, Klebsiella pneumoniae, Bacillus cereus, Pseudomonas putida* and *Salmonella paratyphi* were taken for the test. Some of the tested compounds were found to be toxic against the bacteria.

KEYWORDS

Antibacterial activity;
1,8-naphthyridines containing azetidinones;
Thiazolidinones;
2,4-dihydroxy 1,8-naphthyridine.

INTRODUCTION

The 1,8-naphthyridine group of compounds have been proved to be active antibacterial agents[1-3]. 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[4]. The antimicrobial activity[5] of 1,8-naphthyridine derivatives. 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[6] 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 ant malarial[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 antibacterial activity of newly synthesized 1,8-naphthyridine containing Azetidinones, Thiazo-lidinones,2,4-dihydroxy 1,8-naphthyridine. 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 were screened for their *in vitro* antibacterial activity against *Staphylococcus aureus, Klebsiella*

pneumoniae, Bacillus cereus, Pseudomonas putida and *Salmonella paratyphi*.Tetracycline 100 µ g/ml was dissolved in 5 % aqueous DMF and used..The results were recorded in duplicate.

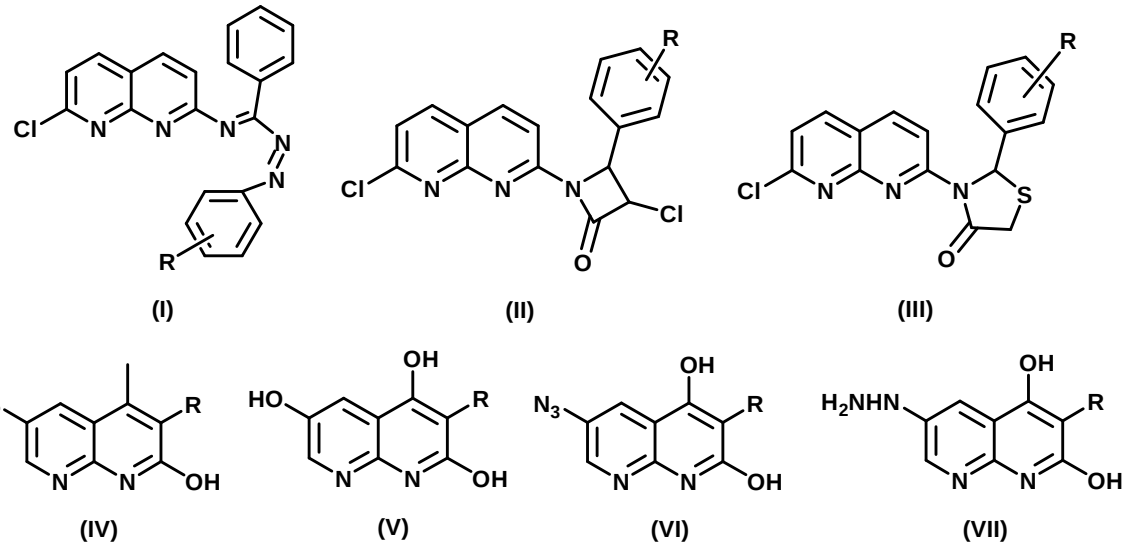

TABLE 1 : Effect of the synthesized compounds I (a-e), II (a-e) and III (a-e) on five bacteria.

Compound No	R	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Bacillus cereus*	*Pseudomonas putida*	*Salmonella paratyphi A*	*Salmonella paratyphi B*
I a	-H	4	3	7	1	1	2
I b	4-OMe	19	15	12	17	9	8
I c	2-OH	10	11	8	9	5	4
I d	4-Cl	18	15	11	15	7	9
I e	3-OH, 4-OMe	20	17	16	16	8	9
II a	-H	9	6	8	1	-	1
II b	4-OMe	10	9	18	5	-	1
II c	2-OH	5	4	6	5	1	2
II d	4-Cl	8	7	12	6	1	1
II e	3-OH, 4-OMe	12	11	13	7	2	3
III a	-H	6	4	1	1	1	2
III b	4-OMe	10	9	8	4	3	2
III c	2-OH	8	5	2	3	1	2
III d	4-Cl	10	8	6	4	2	3
III e	3-OH, 4-OMe	12	11	15	9	2	4
Tetracycline		25	18	20	19	16	21

RESULTS AND DISCUSSION

The antibacterial activity of all the substituted 1,8-naphthyridine derivatives were determined against five bacteria strains. Their possible antibacterial activity are reported in TABLE 1 and TABLE 2. Perusal of the above TABLE 1 reveals that antibacterial activity of the derivatives having methoxy as substituent is more toxic than simple hydroxy compound and chloro compound to all five bacteria. Thiazolidinones and aziditazones derivatives were also toxic towards all bacteria. Compound **(Ie)**, **(Id)** and **(Ib)** were more toxic towards *Staphylocccus aureus* and *Klebsiella*,

TABLE 2 : Effect of the synthesized compounds IV (a-c), V (a-c),VI (a-c) and VI (a-c) on five bacteria.

Compound No	R	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Bacillus cereus*	*Pseudomonas putida*	*Salmonella paratyphi A*	*Salmonella paratyphi B*
IV a	-H	6	5	3	6	2	-
IV b	$-CH_3$	6	4	4	6	2	1
IV c	$-CH_2$-Ph	7	5	5	6	1	2
V a	-H	2	-	5	2	3	-
V b	$-CH_3$	2	-	9	3	4	-
V c	$-CH_2$-Ph	4	2	10	3	5	1
VI a	-H	6	2	1	5	5	1
VI b	$-CH_3$	10	3	1	5	4	2
VI c	$-CH_2$-Ph	12	4	2	7	7	1
VII a	-H	5	-	6	5	3	-
VII b	$-CH_3$	5	1	7	7	4	1
VII c	$-CH_2$-Ph	7	1	9	9	5	2
Tetracycline		25	18	20	19	16	21

Pseudomonas, *Bacillus cereus* Compounds **(IIa)** and **(IIb)** were not effective against *Salmonella* group of organisms.

Perusal of the above TABLE 2 reveals that the derivatives **(Vc)**, **(VIb)**, **(VIc)** and **(VIIc)** more toxic to all five bacteria. The compound which has methyl group and benzyl group is more toxic than simple naphthyridine system. Azido substituent has shown toxicity to bacteria except *Salmonella paratyphi B* and *Klebsiella pneumonia*. Thio and hydroxy substituted derivatives are also more toxic towards all bacteria. The compounds which have hydrazine substituent have shown versatile toxicity to all bacteria. Compounds **(VIb)** and **(VIa)** showed good activity against Staphylococcus *aureus*. All the compounds synthesized did not show much activity against Salmonella paratyphi B.

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