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Antimicrobial activity of oxadiazole, thiazolidin-4-one and azetidin-2-one derivatives of 1*H*-Imidazo[4,5-b]pyridine.

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ABSTRACT

The effect of substituted 1*H*-Imidazo[4,5-b]pyridine derivatives has been investigated for their antibacterial activity on different bacteria and fungi by well diffusion method. Six bacteria, *viz Staphylococcus aureus, Micrococcus luteus, klebsiella pneumoniae, Salmonella paratyphi A, Salmonella paratyphi B,* and *Escherichia coli* were taken for the test. Some of the compounds tested were found to be toxic against the bacteria.

Keywords: antimicrobial, oxadiazole, pyridine.

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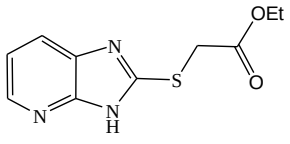
INTRODUCTION

1*H*-Imidazo[4,5-b]pyridine derivatives are important class of heterocyclic compounds and these derivatives attracted many researchers as they show wide range of biological activity. The present study has been aimed at showing antimicrobial activity of newly synthesized 1*H*-Imidazo[4,5-b]pyridine derivatives. The studies have demonstrated [1] that the stability of these materials towards the major pathways of nucleoside inactivation, e.g., deamination by adenosine deaminase and glycosidic cleavage by nucleoside phosphorylases, are important factors in the design of therapeutic agents. For these reasons, benzimidazole based nucleosides have been prepared and evaluated [2,3] as antiviral drugs. Synthetic nucleosides containing the 7-amino-imidazo[4,5-b]pyridine nucleus (i.e., the 1-deazapurines) have already been employed in numerous chemotherapeutic applications [4]. Substituted benzimidazoles and structurally related compounds are of pharmacological and therapeutical interest [5]. In some cases, bioisosteric replacement within the benzimidazole scaffold leading to imidazo[4,5-b]pyridines resulted in improved properties as compared to the corresponding parent compound [6]. Imidazo[4,5-b]pyridines are important class of biologically active compounds showing high affinity to corticotropin-releasing factor [5] and anticancer, [7] antiviral, [8] antimitotic, [9] and also tuberculostatic action [10] depending on the nature and position of substituents on the heterocycle. In addition, certain members of this class display high affinity for the AT1 receptor and are thus potent nonpeptide angiotensin II antagonists [11]. A practical asymmetric synthesis of a novel aminopiperidine-fused imidazopyridine dipeptidyl peptidase IV (DPP-4) inhibitor has been developed [12].

Oxadiazole, Thiazolidin-4-one and Azetidin-2-one derivatives of 1*H*-Imidazo [4,5-b]pyridine



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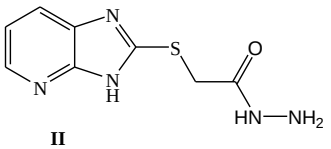

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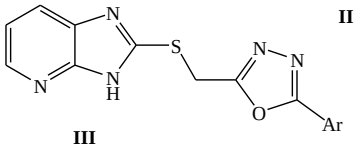

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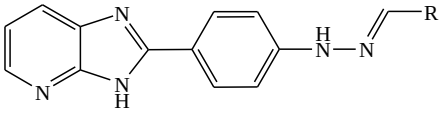

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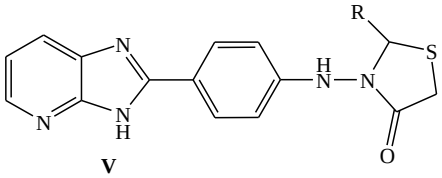

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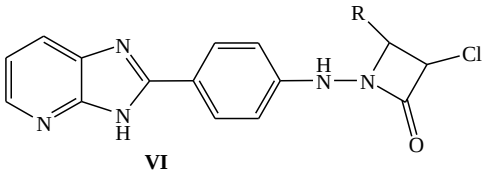

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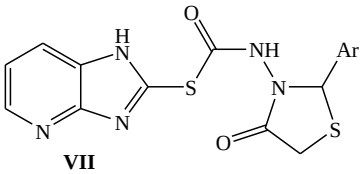

VII

MATERIAL AND METHODS

All the compounds were screened for their *in vitro* antibacterial activity against *Staphylococcus aureus, Micrococcus luteus, klebsiella pneumoniae, Salmonella paratyphi A, Salmonella paratyphi B,* and *Escherichia coli*. Tetracycline (100 µ g/ml) was used as a standard drug for comparison. The zone of inhibition was given in millimeters (mm). All the compounds were dissolved in 5 % aqueous DMF and used for testing their activity.

The stock solution for each of the test compounds was prepared by dissolving 10 µg/ml of it in 10 ml of ethyl alcohol and different concentrations were obtained by diluting with distilled water. The solvents treated in a similar manner without any test compound served as control. The spore germination was so

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adjusted as to appear 30-40 spores per microscope field (H.P). The experiment was conducted in quadruplicate and repeated at least three times. The controls and treatments were incubated at room temperature (27 ± 20C) for 24 hours. At the end of incubation period, the numbers of spores germinated were counted to calculate the percentage of spore germination.

Table 1: Antibacterial activity of 4-(3H-imidazo[4,5-b]pyridin-2-yl)phenylamino)-2-arylthiazolidin-4-ones, 1-(4-(3H-imidazo[4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4-arylazetidin-2-ones

Compound	*S.aureus*	*E.Coli*	*Klebsiella pneumoniae*	*Salmonella paratyphi A*	*Salmonella paratyphi B*	*Micrococcus luteus*
I	4	3	7	1	1	2
II	9	6	18	1	--	1
III a	6	4	1	1	1	2
III b	10	8	6	4	2	3
III c	12	11	15	9	2	4
III d	9	8	6	5	1	2
III e	10	9	5	6	2	3
Tetracycline	25	15	18	16	10	17

a = phenyl, b = 3-methoxyphenyl, c= 4-chlorophenyl, d= 4-methylphenyl, e= 4-nitro phenyl
***** Inhibition zone in mm (-- indicates no inhibitory activity)
Control inhibition zone (which indicates inhibition zone of solvent) was subtracted from inhibition zone of compounds which gives actual inhibition zone of compounds.

Table 2: Antibacterial activity of S-(1H-imidazo[4,5-B]pyridin-2-yl)carbo2-arylthiazolidin-4-ones

Compound	*S.aureus*	*E.Coli*	*Klebsiella pneumoniae*	*Salmonella paratyphi A*	*Salmonella paratyphi B*	*Micrococcus luteus*
IV a	8	7	7	6	1	1
IV b	12	11	13	7	2	3
IV c	6	4	1	1	1	2
IV d	17	7	5	1	6	13
IV e	1	8	3	2	1	1
V a	5	6	4	1	1	2
V b	2	5	1	2	1	1
V c	1	8	2	1	1	3
V d	2	10	2	1	2	3
V e	1	12	1	1	2	3
VI a	8	7	7	6	1	1
VI b	12	11	13	7	2	3
VI c	6	4	1	1	1	2
VI d	17	7	5	1	6	13
VI e	1	8	3	2	1	1
Tetracycline	25	15	18	16	10	17

a= Phenyl, b= 3-Chlorophenyl, c= 4-Chlorophenyl, d= 2-chlorophenyl, d= 4-methoxyphenyl
*****Inhibition zone in mm (- indicates no inhibitory activity)
Control inhibition zone (which indicates inhibition zone of solvent) was subtracted from inhibition zone of compounds which gives actual inhibition zone of compounds.

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Table 3: Antibacterial activity of s-(1H-imidazo[4,5-b]pyridin-2-yl)carbo2-arylthiazolidin-4-ones

Compound	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Salmonella paratyphi A*	*Salmonella paratyphi B*	*Micrococcus luteus*
VII a.	12	2	-	-	8
VII b.	19	5	2	5	9
VII c.	11	2	1	-	7
VII d.	15	3	1	1	7
VII e.	10	4	3	2	8
Tetracycline	25	18	16	10	17

*****Inhibition zone in mm (- indicates no inhibitory activity)
Control inhibition zone (which indicates inhibition zone of solvent) was subtracted from inhibition zone of compounds which gives actual inhibition zone of compounds.

RESULTS AND DISCUSSION

The antibacterial activity of all the substituted 1*H*-Imidazo[4,5-b]pyridines was determined against six bacteria strains. Their antibacterial activities are reported in Table-1, Table-2 and Table-3.

However, table-1 reveals that the derivative having methoxy as substituent is more toxic than simple hydroxy compound and chloro compound to all six bacteria. Among all the compounds, the oxazoles were found to be more toxic than Schiff bases. Schiff bases were also toxic towards all bacteria. The compounds which have methoxy substituent have shown versatile toxicity to all bacteria.

Table-2 shows that the derivative having chlorine as substituent is more toxic to all six bacteria. Among the chloro group compounds, the compound which has methoxy group is more toxic.

Table-3 reveals that the derivative having p-chloro substituent has shown toxicity to bacteria except *Salmonella paratyphi A* and *Klebsiella pneumonia*. The other derivatives are also toxic towards all bacteria.

CONCLUSIONS

Oxadiazole, thiazolidin-4-one and Azetidin-2-one derivatives of 1*H*-Imidazo[4,5-b]pyridine were screened and achieved good results. The method adopted is operationally simple, easer work-up and are environmentally benign processes. Moreover, pyridines are used as pharmaceutical drugs. The screening of the compounds for bioactivity is underway and genuine.

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