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SYNTHESIS OF SOME PYRIMIDINE DERIVATIVES AND EVALUATION OF THEIR ANTIBACTERIAL ACTIVITES

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ABSTRACT

Antimicrobial agents play key role in the management of infections. Challenges faced by the chemists to develop a wide spectrum antimicrobial agent were the antibiotic resistance occurred due to the misuse of these agents. Pyrimidine is prevalent in numerous natural products and posses a wide range of biological activities. The work includes the synthesis of some 1,3-dihydro pyrimidine derivatives from different substituted aldehydes. Pyrimindine derivatives (6a,6b,6d) were synthesized from different aromatic aldehydes and screened for their antimicrobial properyies in gram positive (*Bacillus subtitis, Staphylococous aureus*) and gram negative (*Pseudomonas aeruginosa, Escherichia coli*) organisms at concentration 400µg/disc and 200µg/disc. The compound 6b (phenyl derivative) have significant antimicrobial properties than other synthesized derivatives.

Key words: Purines, Pyrimidines, substituted aldehydes, antibacterial.

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INTRODUCTION

Antimicrobial agents play key role in the management of infections. Many types of antimicrobials with different mechanism of action, pharmacological properties and spectra of activities are available in market. Challenges faced by the chemists to develop a wide spectrum antimicrobial agent were the antibiotic resistance occurred due to the misuse of these agents. Pyrimidine (Fig-1) is a heterocyclic aromatic compound similar to pyridine, containing a totally unsaturated six membered ring with nitrogen at 1, 3-position. It is prevalent in numerous natural products With effective antibacterial properties. The work highlights the synthesis of some pyrimidine derivatives and screening of the synthesized compounds for their antimicrobial action (1, 2).

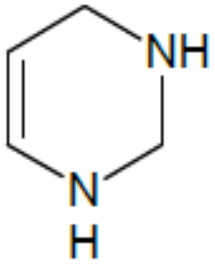
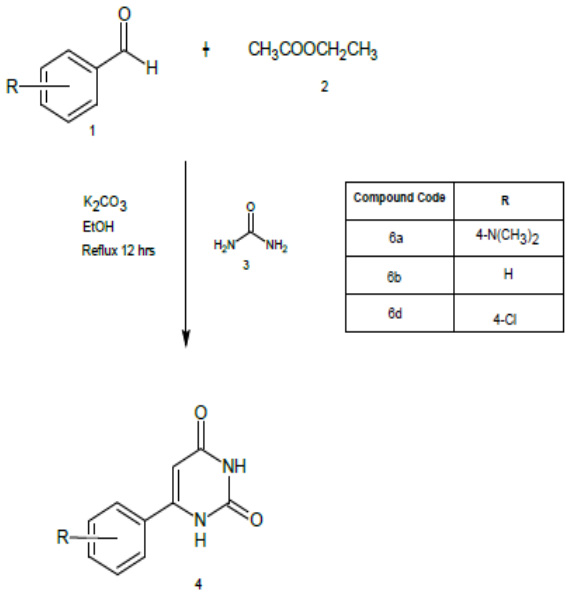


Fig-1 Structure of 1, 3-Dihydropyrimidine

Scheme of synthesis of pyrimidine derivatives

A mixture of ethyl acetate (50millimole), urea (50milimole), substituted aldehydes (50millimole) and potassium carbonate (50millimole) in absolute alcohol

(50ml) was refluxed for 12 hours and the mixture was neutralized with glacial acetic acid. The resultant mixture was poured into crushed ice. The precipitate was filtered, washed with water, dried and recrystallised from absolute ethanol (Fig-2).



***(1)-substituted aldehydes , (2) -ethyl acetate, (3)-urea , (4)- Product**

Fig-2 scheme of synthesis of pyrimidine derivatives

Derivatives named 6a, 6b and 6d are prepared through above procedures with reasonable good yields. The structure of the derivative 6d was confirmed by IR spectra studies.

Antimicrobial Screening

The organisms (*Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa*) were inoculated in the Mueller Hinton agar plates. It was allowed to dry at room temperature. The sterile discs containing test compounds (6a,6b,6d), standard and control were placed on the solid medium and incubated for 18-24hrs. Observations were made for zone of inhibition around the test and compared with that of standard (3, 4).

RESULT AND DISCUSSION

The synthesized compounds are crystalline solid and the features of derivatives synthesized are shown in the table-1.

Table-1 Chemical properties of synthesized compounds

Compound	R	Molecular weight (gm)	Percentage yield(%w/w)	Melting point (ºC)
6a	4-N(CH3)2	231.25	72	130
6b	H	222.63	76	140
6d	4-Cl	228.63	82	132

The suggested groups of the derivative 6d were confirmed by IR Spectra shown in the figure:3 (presence of Absorption maxima at 3300cm^{-2} (-NH2 Stretching), 1238cm^{-2}(C-N Stretching), 1593cm^{-2} (C=C Stretching), 1635cm^{-2} (C=O Stretching), 814cm^{-2} (C-Cl Stretching)) (5, 6) (Fig-3).

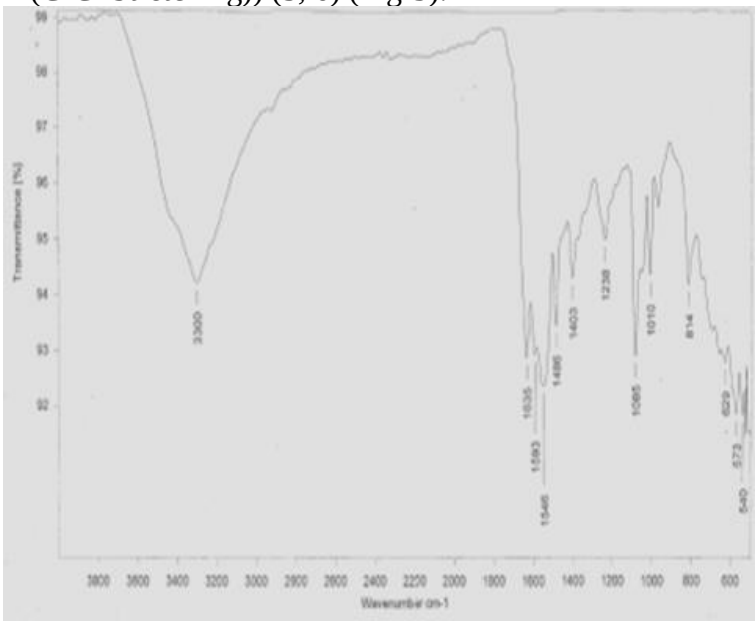


Fig- 3 IR Spectra of Compound 6d

Antimicrobial Screening

The synthesized derivatives were screened for anti microbial activity. The results were shown in the table-2 and fig- 4 and 5.

Table-2 Zone of inhibition in bacterial strains

Compound Code	Diameter of zone of inhibition in mm							
	Staphylococcus aureus		***Bacillus subtilis***		***Escherichia coli***		***Pseudomonas aeruginosa***	
	200µg/disc	**400 µg/disc**	**200µg/disc**	**400 µg/disc**	**200 µg/disc**	**400 µg/disc**	**200 µg/disc**	**400 µg/disc**
6a	10	12	18	20	9	9	12	15
6b	-	-	13	15	-	-	-	-
6d	9	10	-	-	-	-	-	-
Standar Cipro Floxacin (5µg/disc	25	26	28	36	25	26	32	36

Note- Solvent used: DMSO, (-) indicates no zone of inhibition, (Diameter of zone of inhibition: 17 mm & above: Sensitive, 13-16mm: Moderately sensitive, <12 mm: resistant).

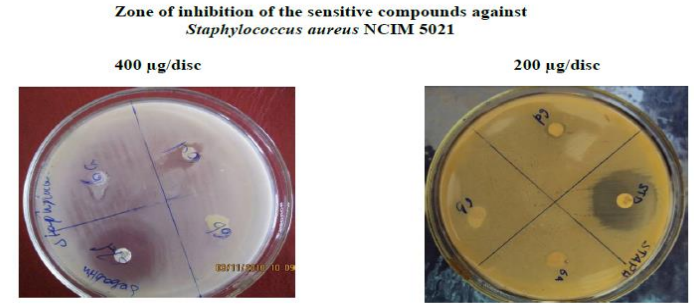
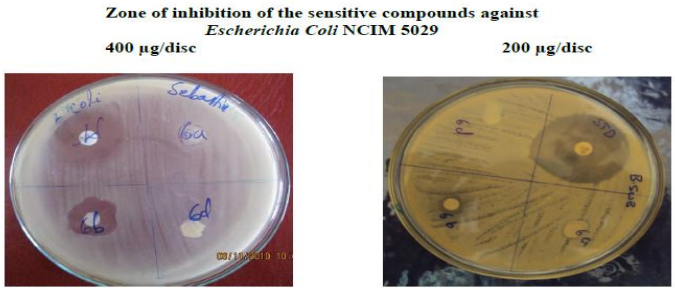


Fig-4 Zone of inhibition of gram positive bacterial strains



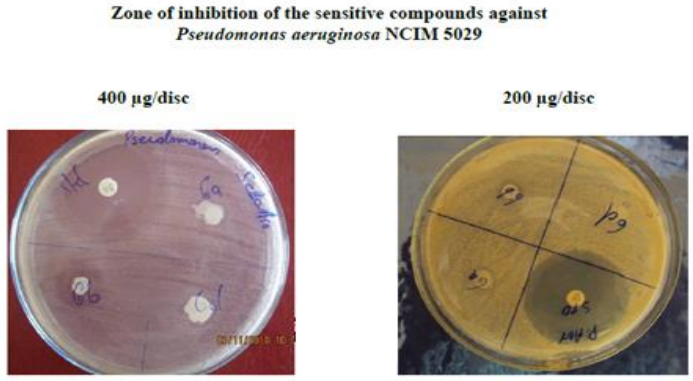


Fig- 5 Zone of inhibition of gram negative bacterial strains

The compound 6b (phenyl derivative) moderately sensitive to *Bacillus subtilis* and sensitive to *Escherichia coli* and *Pseudomonas aeruginosa* at 400µg/disc. Other compounds are inferior in activity.

CONCLUSION

Pyrimindine derivatives (6a, 6b, 6d) were synthesized from different aromatic aldehydes. The synthesized derivatives were screened for their antimicrobial properties in gram positive (*Bacillus subtitis, Staphylococous aureus*) and gram negative (*Pseudomonas aeruginosa, Escherichia coli*) organisms at 400µg/disc and 200µg/disc. The compound 6b (phenyl derivative) have significant antimicrobial properties.

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