AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Synthesis and Antibacterial Activity of Pyrimidine Derivatives of 1,3-Dihydropyrimidine

Sebastin V[1], Sarath lal P.S[1],Arun Ramachandran[1], Sumayya C. H[1].

1. Department of Pharmaceutical Chemistry, Malik Deenar College of Pharmacy, Seethangoli, Kasaragod, Kerala.

ABSTRACT

Purines and pyrimidine derivatives are the important class of compounds in medicinal chemistry. Pyrimidine – a totally unsaturated six membered ring containing nitrogen at 1,3-position. They represent the diazine family with urazil and thymine being the constituents of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) and with cytosine. The work highlights one pot synthesis of some 1,3-dihydro pyrimidine derivatives from different substituted aldehydes. All the synthesized derivatives were screened for antibacterial activity using gram positive (*Bacillus subtilis*, *Staphylococcus aureus*) and gram negative (*Pseudomona aeruginosa*, *Escherichia coli*) organisms at concentrations of 400µg/disc and 200µg/disc. The compound 5b (p-dimethyl aminophenyl derivative) was found to be sensitive in all strains. The structure of compound 5b was confirmed by IR spectral studies.

Keywords: Dihydropyrimidine, substituted aldehydes, antibacterial, IR spectra

*Corresponding Author Email: sarathlaalu@gmail.com

Received 24 July 2017, Accepted 12 August 2017

Please cite this article as: Sebastin V *et al*., Synthesis and Antibacterial Activity of Pyrimidine Derivatives of 1,3-Dihydropyrimidine. American Journal of PharmTech Research 2017.

INTRODUCTION

Drug discovery involves the identification, synthesis and development of new chemical entities suitable for therapeutic use. Chemists mainly focus on heterocyclic compounds to design effective drugs and diagnostic agents. Their structural subunits exist in many natural products such as hormones, vitamins and antibodies[1]. Purine and pyrimidine derivatives are the important class of compounds in medicinal chemistry. Pyrimidine – a totally unsaturated six membered ring contains nitrogen at 1st and 3rd positions. It represents the diazine family and its derivatives uracil, present in RNA and thymine in DNA while cytosine is present both in RNA and DNA. However the current study intends to focus on the synthesis of pyrimidine class of antimicrobial agents to facilitate the development of more potent as well as effective antibacterial agents[2,3].

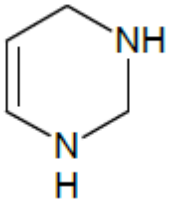
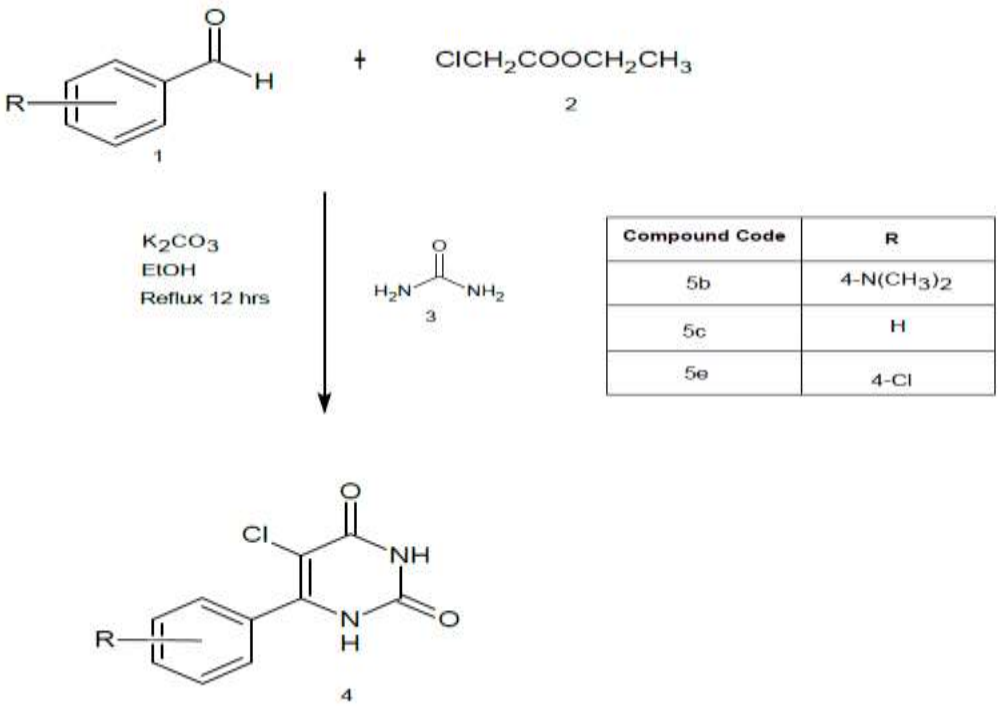


Figure 1: 1, 3-Dihydropyrimidine

General procedure for the synthesis of 1,3- dihydropyrimidine derivatives:

A mixture of ethyl chloro acetate (0.5M), urea(0.5M), substituted aldehydes (0.5M) and potassium carbonate (0.5M) in absolute alcohol (50ml) was refluxed for 12 hours and the mixture was neutralized with glacial acetic acid. The resultant mixture was poured in crushed ice. The product (4) was filtered, washed with water and recrystallised with ethanol.



Compound Code	R
5b	4-N(CH3)2
5c	H
5e	4-Cl

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

Figure 2 scheme of synthesis of 1,3- dihydropyrimidine derivatives

Derivatives named 5b, 5c and 5e are prepared through above procedures with reasonable good yields. The structure of the derivative 5b was confirmed by IR spectra studies.

Antimicrobial Screening (Kirby-Bauer Method)

The organisms (*Staphylococcus aureus , Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa*) was inoculated in the Mueller Hinton agar plates. It was allowed to dry at room temperature. The sterile discs containing test compounds (5b, 5c, 5e), standard and blank 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[4,5].

RESULTS AND DISCUSSION

The compounds synthesized are in solid stage and suggested groups of the derivative 5b were confirmed by IR Spectra (presence of Absorption maxima at 3284cm^{-2} (-NH2 Stretching), 1226cm^{-2}(C-N Stretching), 1578cm^{-2} (C=C Stretching), 2364cm^{-2} (C=O Stretching), 805cm^{-2} (C-Cl Stretching))[6,7].

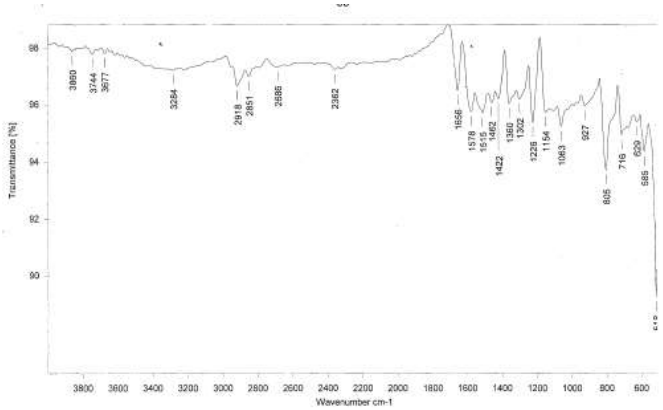


Figure: 3 IR Spectra of Compound 5b

Table: 1 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	**400µg/disc**	**200µg/disc**	**400µg/disc**	**200µg/disc**	**400µg/disc**	**200µg/disc**	**400µg/disc**
5b	10	12	18	20	9	9	12	15
5c	-	-	13	15	-	-	-	-
5e	9	10	-	-	-	-	-	-
Standard Ciprofloxacin (5µg/disc)	25	26	28	36	25	26	32	36

Solvent used: DMSO,

(-) indicates no zone of inhibition,

(Diameter of zone of inhibition:17 mm & above: Sensitive, 13-16mm: Moderately sensitive, <12 mm: resistant).

Zone of inhibition of the sensitive compounds against *Staphylococcus aureus* NCIM 5021

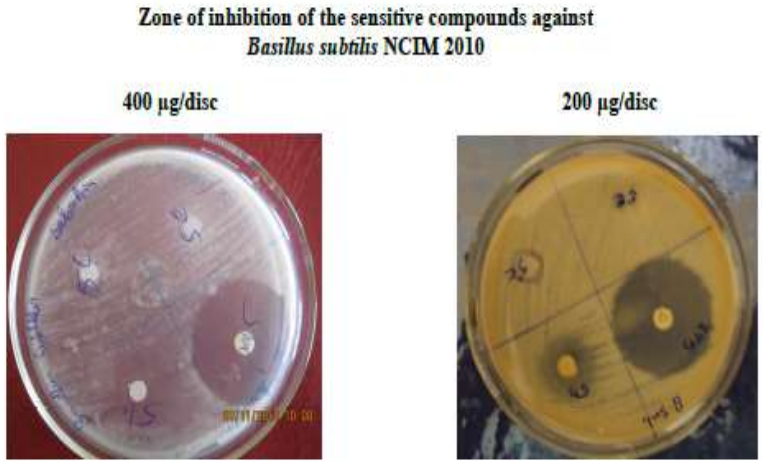


Figure :4 Zone of inhibition of gram possitive bacterial strains

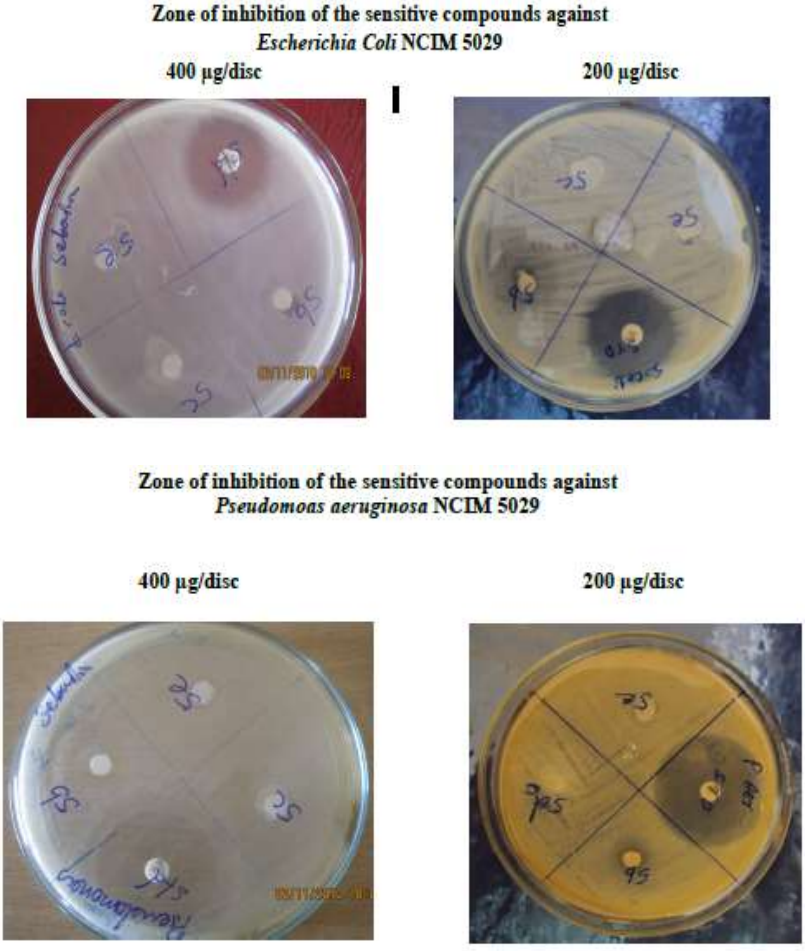


Figure: 5 Zone of inhibition of gram negative bacterial strains

The compound 5b (p-dimethyl aminophenyl derivative) was moderately sensitive against *staphylococcus aureus* and *Pseudomonas aeruginosa.* and sensitive against *Bacillus subtilis*. The compound 5c (phenyl derivatives) was moderately sensitive against *Pseudomonas aeruginosa.*

CONCLUSION

The work highlights the one pot synthesis of some 1,3-dihydro pyrimidine derivatives from different substituted aldehydes. All the synthesized derivatives were screened for gram positive (*Bacillus subtilis, Staphylococcus aureus*) and gram negative (*Pseudomona aeruginosa, Escherichia coli*) organisms at 400µg/disc and 200µg/disc. The compound 5b (p-dimethyl aminophenyl derivative) was found to be sensitive in all strains.

REFERENCE

1. Finar I.L. Organic Chemistry. Pearson education, Asia, 6th edition. 827.
2. Nelson D.L, Michael M.C. Principles of Biochemistry. Freeman And Company. 5th edition, (2008).272-274
3. Basavaraj P. Organic Synthesis.4th edition,(1963), 182.
4. Ronald N.A, Lawrence C.P, Alfred E.B. Laboratory Manual of Experimental Microbiology. Mosby publishers, 14th edition.5-35
5. Mackie, M.C Cartnay. Practical Medical Microbiology. Churchill Livingstons,14th edition.95-130
6. Sharma B.K. Spectroscopy. Goel publishing House,193.
7. Kemp W. Organic Spectroscopy, Palgrave,3rd edition,58.