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Research Article

ANTIBACTERIAL SCREENING OF PYRIMIDINE-CARBONITRILES

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ABSTRACT

In the present study, we have reported *in vitro* antibacterial activity of our earlier reported compounds by serial dilution method. Among the compounds tested, few were found to be most effective antibacterial agents. Compounds containing thiazolo and quinolone ring may imparts better activity. The hydrazine substitution on pyrimidine may be responsible for reducing the activity. The results revealed that the synthesized compounds may be helpful to find out potential lead for future drug discovery.

Keywords: Pyrimidine; Antibacterial activity; Thiazolo; Quinolone; Hydrazine; Minimum inhibitory concentration.

INTRODUCTION

Pyrimidine, being an integral part of DNA and RNA, imparts diverse pharmacological properties such as effective bactericide and fungicide[1,2]. Certain pyrimidine derivatives are also known to possess antimalarial[3], antifilarial[4], antibacterial, antifungal[5-6], anticonvulsant[7]and antihistamine[8] activity. Some of the 3,4-dihydropyrimidines (DHPM) have emerged as integral backbones of several calcium channel blockers, antihypertensive agents, adrenergic and neuropeptide antagonist[9]. Several natural marine products containing the 3,4–dihydropyrimidine core have been reported in the literature with interesting biological activities such as the anti-HIV alkaloid batzelladine B[10,11].

Fused pyrimidine derivatives have attracted attention of numerous researchers over many years, due to their important biological activities. Preclinical data from literature survey indicated that the heterocyclesin association with the pyrimidine has shown good antimicrobial[12-14], antioxidant[14], antitumour[15], analgesic, anti-inflammatory[16,17] and antipyretic[17] activities. In particular, pyrimidines[18-23] derivativeswere found as potent antimicrobial agents.

Motivated by the above mentioned findings and on continuation of our investigation[24], to discover new potentially active agents, we have evaluated our earlier reported[25] compounds for their *in vitro* antibacterial activity (MIC) by serial dilution method.

MATERIALS AND METHODS

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification.

ANTIBACTERIAL ACTIVITY (MINIMUM INHIBITORY CONCENTRATION) BY SERIAL DILUTION METHOD

The minimum inhibitory concentration of the compounds was determined in Nutrient broth (NB) for bacteria [Gram-positive bacteria [*Bacillus subtilis* (NCIM 2546) and *Staphylococcus aureus* (NCIM 2120)] and Gram-negative bacteria [*Pseudomonas aeruginosa* (MTCC 2488) and *Escherichia coli* (NCIM 2065)] by the serial dilution method.[26-28] Seeded broth (broth containing microbial spores) was prepared in NB with 24 h old bacterial cultures on nutrient agar (Hi-media, India) at 37 ± 1 ^{o}C. The bacterial suspension was adjusted with sterile saline to a concentration of 1 × 10^4–10^5 CFU. All the compounds were screened for their antibacterial activities in triplicate sets at different concentrations (1000, 500, 250 and 200 µg/mL).

The compounds which were found to be active in primary screening were further diluted to obtain 100, 50, and 25 µg/mL concentrations. The compounds which were found to be inactive in primary screening were further screened at higher (1250, 1500, 1750 and 2000 µg/mL) concentrations. The tubes were incubated in BOD incubators at 37 ± 1 ^{o}C for bacteria. The Minimum Inhibitory Concentration (MIC) was recorded by visual observation after 24 h (for bacteria) of incubation. The lowest concentration, which has shown no growth after spot subculture was considered as MIC for each compound. The highest dilution showing at least 99 % inhibition was taken as Minimum Inhibitory Concentration (MIC). Streptomycin was used as standards for bacterial study.

RESULTS AND DISCUSSION

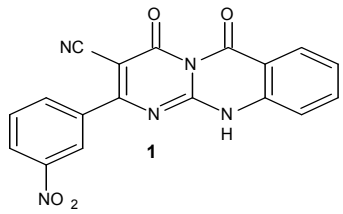
Antibacterial activity

The reported compounds were screened for their antibacterialactivity against bacteria such as, *Bacillus subtilis* and *Staphylococcus aureus* (Gram-positive bacteria) and *Pseudomonas aeruginosa* and *Escherichia coli* (Gram-negative bacteria). The results of preliminary antibacterial testing of the compounds were reported as minimum inhibitory concentration (Table 1). The results of preliminary antibacterial testing revealed that compounds **1** and **2** are showing good activity against*E. coli* and *P. aeruginosa*. Remaining all the other compounds has shown moderate activity against these species. All the compounds has shown moderate to weak activity against *B. subtilis* and *S. aureus*.

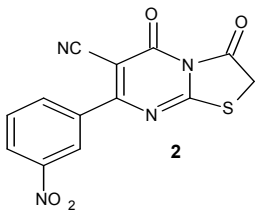
Amongst all the tested compounds, 1 and 2 have shown good activity than remaining derivatives. The activity observed in current study is comparable with earlier reported zone of inhibition against same species of bacteria. No compound has shown better activity than standard, streptomycin.

Table 1: Antibacterial activities of compounds

Compounds	Minimum Inhibitory Concentration (µg/mL)			
	Gram-negative bacteria		Gram-positive bacteria	
	E. coli	*P. aeruginosa*	*B. subtilis*	*S. aureus*
1	100	200	250	250
2	100	200	250	500
3a	250	500	750	750
3b	250	250	250	500
3c	200	250	250	250
3d	250	500	500	750
Streptomycin	50	50	50	50



1



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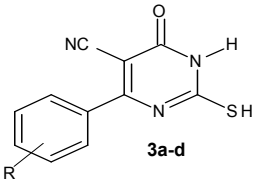

3a-d

	R
3a	3-OH
3b	4-OH
3c	3-NO$_2$
3d	4-NO$_2$

Figure 1: Structure of the compounds

CONCLUSION

In conclusion, we have described investigation of selected compounds for their *in vitro* antibacterial activities against *Bacillus subtilis*, *Staphylococcus aureus*,*Pseudomonas aeruginosa*and*Escherichia coli*. In the newly synthesized compounds, it is clear that the highest antibacterial activity was observed in compounds **1** and **2**. This may be due to thaizolo and quinolone ring fused to pyrimidine ring.Polar substitution like hydrazine may reduce the antibacterial activity. To summarize with, we found that the novel class of pyrimidines have emerged as a valuable lead. Few of synthesized compounds might be useful as antibacterial agents in future. These new pyrimidine derivatives have proved to be promising candidates for further efficacy evaluation.

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