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Short Communication

ANTIBACTERIAL AND ANTIFUNGAL STUDIES 5-ETHOXYCARBONYL-4-ARYL-6-METHYL-3, 4-DIHYDROPYRIMIDINONES

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Abstract: Seven 5-ethoxycarbonyl-4-aryl- -6-methyl-3,4-dihydropyrimidinones **4a–g** are screened for their antibacterial activity against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi* and antifungal activity against *Candida albicans, Aspergillus flavus, Rhizopus* and *Mucor*. Ciprofloxacin is used for the standard for antibacterial and Amphotericin B is used for the standard for antifungal studies. Compounds **4a**, **4b**,**4c, 4d, 4e** and **4f** exhibited excellent *in vitro* antibacterial activity against all the tested organisms. Where as the same set of compounds exerted potent *in vitro* antifungal activity against *Candida albicans, Aspergillus flavus* and *Rhizopus.*

Key words: Antibacterial activity, antifungal activity, Dihydropyrimidinones

INTRODUCTION

Now-a-days sulphur containing compounds possessing diverse type of biological properties cardiovascular activity[1, 2]. Dihydropyrimidine derivatives have a wide range of biological and anti-hypertensive activity[3]. Most notably among them are the batzalladine alkaloids, which have been found to be potent HIV-gp-120-CD4 inhibitors[4]. Dihydropyrimidinones and related compounds exhibit a wide range of biological activities such as antiviral, antitumor, antibacterial and antiinflammatory properties[5]. These observations places new emphasis on the need of as well as search for alternative new and more effective antimicrobial agents with a broad spectrum

The aim of this study was to evaluate the biological activities of dihydropyrimidin-2(1H)-ones **4a–4g**. The results of the antibacterial and antifungal activities are discussed in this paper. To percept structure-activity relationship well, numberings of the target compound is shown below **Fig. 1**.

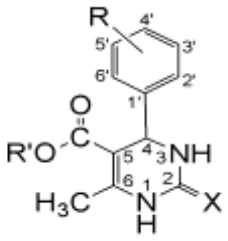

Fig-1: Target compound numbering.

MATERIALS AND METHODS

All the bacterial strains namely *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella typhi* and fungal strains namely *Candida albicans, Aspergillus flavus, Rhizopus* and *Mucor* were obtained from Faculty of Medicine, Annamalai University, Annamalainagar, Tamil Nadu, India.

The compounds were synthesized based on the literature procedure[6]. The *in vitro* antimicrobial activities of the compounds were tested in Sabouraud's dextrose broth (SDB, Hi-media, Mumbai) for fungi and nutrient broth (NB, Hi-media, Mumbai) for bacteria by the twofold serial dilution method[7].

The test compounds were dissolved in dimethyl sulfoxide (DMSO) to obtain 1 mg/ml stock solutions. Seeded broth (broth containing microbial spores) was prepared in NB from 24 h old bacterial cultures on nutrient agar (Hi-media, Mumbai) at 37 ± 1 °C while fungal spores from 24 h to 7-day-old Sabouraud's agar slant cultures were suspended in SDB. The colony forming units (cfu) of the seeded broth were determined by the plating technique and adjusted in the range of 10^4–10^5 cfu/ml. The final inoculum size was 10^5 cfu/ml for the antibacterial assay and 1.1–1.5 × 10^2 cfu/ml for the antifungal assay. Testing was performed at 7.4 ± 0.2. Exactly 0.2 ml of the solution of test compound was added to 1.8 ml of seeded broth to form the first dilution. One ml of this was diluted with a further 1 ml of the seeded broth to give the second dilution and so on until six such dilutions

were obtained. A set of assay tubes containing only seeded broth was kept as control and likewise solvent controls were also run simultaneously. The tubes were incubated in biochemical oxygen demand (BOD) incubators at 37 ± 1 °C for bacteria and 28 ± 1 °C for fungi. The minimum inhibitory concentrations (MICs) were recorded by visual observations after 24 h (for bacteria) and 72–96 h (for fungi) of incubation. Ciprofloxacin was used as a standard for the bacterial study while Amphotericin B was used as a standard for the fungal study.

RESULT AND DISCUSSION

Physical data of the compounds **4a-4g** are given in the **Table 1**.

Table 1.Physical data of compounds 4a-4g

Compound	R	X	Yield (%)	Melting Point ◦C
4a	2-Cl	O	96	201
4b	3-NO_2	O	98	258
4c	3-Br	O	92	245
4d	3-Cl	O	96	250
4e	2-NO_2	O	98	195
4f	3-NO_2	S	94	256
4g	4-OCH_3	S	96	239

In vitro antibacterial and antifungal activity

Compounds **4a–4g** were tested for their antibacterial activity *in vitro* against *Staphylococcus aureus (SA), Escherichai coli(EC), Klebsiella pneumonia(KP), Pseudomonas aeruginosa(PA)* and *Salmonella typhi(ST).* Ciprofloxacin was used as standard drug. Minimum inhibitory concentration (MIC) in µg/ml values shown in **Table 2**.

Table 2. In vitro antibacterial activity of compounds 4a–g

Compound	Minimum Inhibitory Concentration (MIC) in µg/ml				
	SA	*EC*	*KP*	*PA*	*ST*
4a	25	25	50	25	25
4b	6.25	6.25	6.25	12.5	6.25
4c	25	25	25	25	25
4d	25	25	50	25	25
4e	6.25	6.25	6.25	12.5	6.25
4f	3.13	6.25	3.13	3.13	6.25
4g	50	100	100	50	100
Ciprofloxacin	25	25	12.5	25	25

All the 3,4-dihydropyrimidinones **4a–4g** exerted potent antibacterial activity *in vitro* against the tested bacterial strains. Moreover, compounds **4a**, **4b**, **4c, 4d, 4e** and **4f** exerted excellent antibacterial activities against *S. aureus, E. coli, K. pneumoniae, P. aeruginosa* and *S. typhi.*

The *in vitro* antifungal activity of the synthesized compounds **4a–4g** was studied against the fungal strains viz., *Candida albicans (CA), Aspergillus flavuS(AF), Rhizopus* and *Mucor*. Amphotericin B was used as a standard drug. Minimum inhibitory concentration (MIC) in µg/ml values is shown in **Table 3**.

Table 3. In vitro antifungal activity of compounds 4a–g

Compound	Minimum Inhibitory Concentration (MIC) in µg/ml			
	CA	*AF*	*Rhizopus*	*Mucor*
4a	25	50	25	25
4b	6.25	6.25	12.5	6.25
4c	25	25	25	25
4d	25	50	25	25
4e	6.25	6.25	12.5	6.25
4f	3.13	3.13	6.25	3.13
4g	50	100	100	50
Amphotericin B	25	25	50	25

Compounds **4a**, **4b**, **4c, 4d, 4e** and **4f** exhibited excellent antifungal activities against all the tested fungal strains except *Mucor*.

CONCLUSION

Results of this study show that compounds **4a**, **4b**, **4c, 4d, 4e** and **4f** which contain chloro, nitro and bromo moieties exerted excellent antimicrobial activities against the tested organisms. Further development of this group of 3,4-dihydropyrimidinones may lead to compounds with better pharmacological profile than standard drugs and serve as templates for the construction of better drugs to come to blows bacterial and fungal infections.

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