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Short Communication

Screening of Fused Pyrimidines as Antimicrobial Agents: Inhibitory Activities of Some Tetrahydrobenzothieno-Pyrimidines

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Abstract. Seven synthetic tetrahydrobenzothieno fused pyrimidine derivatives were investigated for their antibacterial and antifungal activities. Their comparative ability to inhibit growth of bacterial species *Bacillus subtilis*, *B. megaterium, Staphyllococcus aureus*, *Salmonella typhi* and *Escherichia coli* in comparison with the commercial antibiotic brand Ampicillin, and of fungal species *Verticillium* sp., *Fusarium solanae, Aspergillus* sp., and *Penicillium* sp., in comparison with the commercial antifungal brand Nystatin is reported.

Keywords: fused pyrimidines, thienopyrimidines, antimicrobial activity

Pyrimidine derivatives, which constitute a partial structure of the purine base and many biologically active compounds, are involved widely in living organisms and have attracted much attention from the view point of medicinal chemistry. The soporific and hypnotic barbiturates and a number of antibacterial and antimalarial drugs also contain pyrimidine rings (Burger, 1960). Some of thienopyrimidine derivatives are reported as potential chemotherapeutic agents (Ram *et al.,* 1981). In a programme to obtain new potent antimicrobial agents, the synthesis of some tetrahydrobenzothieno fused pyrimidine derivatives has been reported earlier (Rahman *et al.,* 2000). The present work describes their antimicrobial activity.

Compounds for antimicrobial screening. Seven compounds studied for the purpose were: 4-amino-5,6,7,8-tetrahydrobenzothieno[2,3-d]pyrimidine(**1**), m.p. 226-227 °C; 8,9,10,11-tetrahydrobenzothieno[3,2-e]imidazo[1,2-c] pyrimidine (**2**), m.p.187-190 °C; 4-amino-2-phenyl-5,6,7,8-tetrahydrobenzothieno[2,3-d]pyrimidine (**3**), m.p. 224-225 °C; 5-phenyl-8,9, 10,11-tetrahydrobenzothieno[3,2-e]imidazo[1,2-c] pyrimidine (**4**), m.p. 183-185 °C; 5,6,7,8-tetrahydrobenzothieno[2,3-d] pyrimidine-2,4 (1*H*,3*H*)-dithione (**5**), m.p. 250 °C (decomposed); 4-amino-5,6,7,8-tetrahydrobenzothieno[2,3-d] pyrimidin-2(1*H*)-thione (**6**), m.p. 228-230 °C; and 3-tosyl-5, 6,7,8-tetrahydrobenzothieno[2,3-d]pyrimidine-4(3*H*)-one (**7**), m.p. 110-112 °C (Fig. 1).

Antimicrobial activity trials. The fused pyrimidine compounds (**1**-**7**) were screened for antibacterial activity (Table 1) against three gram-positive bacteria, *Bacillus subtilis, B. megaterium, Staphylococcus aureus* and two gram-negative bacteria *Salmonella typhi* and *Escherichia coli* using disc diffusion method (Bauer *et al.,* 1966). These compounds (**1**-**7**) were also screened for antifungal activity (Table 2) against four phytopathogenic fungi, *Verticillium* sp., *Fusarium solane, Aspergillus* sp., and *Penicillium* sp., using poisoned food technique (Grover and Moore, 1962). Commercial antibacterial and antifungal brands, respectively, Ampicillin and Nystatin were also tested under similar conditions for comparison.

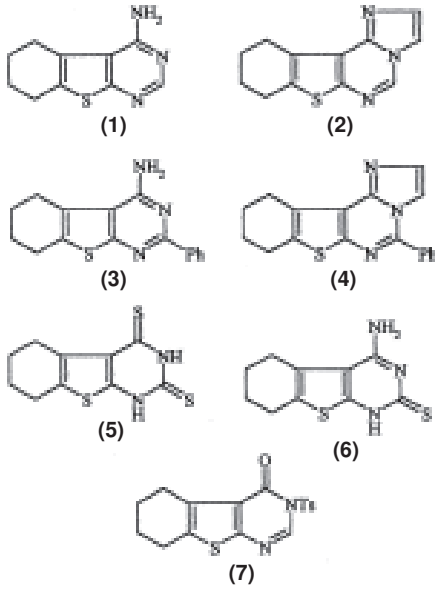

Fig. 1. Structures of fused pyrimidine compounds **(1-7).**

Compound **(5)** showed the highest antibacterial activity against *B. subtilis, Staph. aureus, Salm. typhi* and *E. coli*. Compound **(1)** showed the highest activity against *B. megaterium.* The other compounds also showed weak to moderate activity against all the tested bacteria. The antibacterial activities of

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Table 1. Antibacterial screening of the fused pyrimidine compounds **(1-7)**

Bacterial species	Diameter of zone of inhibition in mm (100 µg (dw)/disc)							
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	Ampicillin 25 µg (dw)/disc
Bacillus subtilis	--	8	--	9	16	14	8	21
B. megaterium	10	6	8	7	8	8	--	20
Staphylococcus aureus	6	9	7	8	10	6	7	19
Salmonella typhi	8	--	6	--	11	7	11	24
Escherichia coli	6	7	6	7	9	6	6	12

--: no inhibition

Table 2. Fungicidal screening of the fused pyrimidine compounds **(1-7)**

Fungal species	% Inhibition of mycelial growth (100 µg (dw)/ml PDA)							
	(1)	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	Nystatin
Verticillium sp.	29	42	49	61	22	13	92	41
Fusarium solane	43	51	41	65	23	26	66	49
Aspergillus sp.	37	36	50	55	17	35	59	45
Penicillium sp.	57	67	67	70	22	46	97	52

all the compounds studied were, however, appreciably less than the commercial brand Ampicillin. For the antifungal activity all the compounds showed good to excellent activity against the tested fungi. Most of the tested compounds were, furthermore, significantly better antifungal agents than the commercial brand Nystatin.

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