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ANTIBACTERIAL AND *IN VIVO* AND *IN VITRO* ANTI-INFLAMMATORY ACTIVITY OF SOME NOVEL SUBSTITUTED THIENOPYRIMIDINONE

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ABSTRACT

3-Amino-2-mercapto-7-methyl-5, 6, 7, 8-tetrahydropyrido (b) thieno [2, 3-d]pyrimidin-4 (3 *H*) -ones were prepared by multi component condensation between sulphur, ketone and ethylcyanoacetate adopting Gewald reaction[1] and then treatment with carbondi sulphide, DMS and NaOH followed by cyclization with hydrazine hydrate. It was condensed with substituted aryl aldehydes to yield Schiff base. Then, these Schiff bases were tested for anti-inflammatory and antibacterial activity.

Key words : Thienopyrimidinone, Antibacterial, Antiinflammatory.

INTRODUCTION

Literature survey reveals that various substituted thienopyrimidines and thienopyrimidinones are known to possess a wide range of pharmacological activities like anti-inflammatory[2, 3], antimalarial[4], antibacterial[5, 6, 7], spasmolytic[8], VEGFR-2 kinase inhibitory activity[9] etc. Earlier, We reported the synthesis and antifungal activity. In continuation of previous work[10], We are reporting the anti-inflammatory and antibacterial screening of title compounds.

EXPERIMENTAL

Antibacterial activity

All the test compounds were assayed *in vitro* for antibacterial activity against two different strain of Gram negative (*E. coli* and *S. typhi*) and Gram positive (*S. aureus* and *B. subtilis*) bacteria using standard protocol[11]. The minimum inhibitory concentration (MIC) was determined by the test-tube dilution technique using Muller-Hinton nutrient broth for

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antibacterial activity. The MIC value was also tested for well known antibiotic like ampicillin to compare the antibacterial activity of these test compounds.

Anti-inflammatory activity

The compounds were also screened for *in vitro* and *in vivo* anti-inflammatory activity by inhibition of bovine serum albumin denaturation[12] and carrageenan induced rat hind paw edema method[13], respectively using ibuprofen as standard drug. The test compounds were dissolved in minimum quantity of water and diluted with phosphate buffer (0.2 M, pH 7.4). Test solution of title compounds were mixed with albumin solution in phosphate buffer and incubated at 27 ±1ºC for 15 min. Denaturation was induced by keeping the reaction mix at 60 ±1ºC in a water bath for 10 min. After cooling, the turbidity of the resulting solution was measured. Average of three readings was taken.

This activity was performed by following procedure of Winter et al.[13] on group of six animals each. Edema was induced in the rats by injecting carrageenan (0.05 mL, 1% (w/v) in. 9% saline) into sub-plantar tissue of the right hind paw. One group was kept as control and treated with propylene glycol. The animal of standard drug and drug treated groups were pretreated with standard drug and test compounds given orally 1 hour before the carrageenan injection, respectively. The paw volume (mL) was measured before carrageenan injection and after with plethysmometer. The percentage anti-inflammatory activity was calculated according to formula given below :

$$\% \text{ Anti-inflammatory activity} = (1- V_t / V_c) \text{ X } 100$$

Where V_t and Vc are the volumes of edema in drug treated and the control groups, respectively. The results are tabulated in Table 1.

Table 1

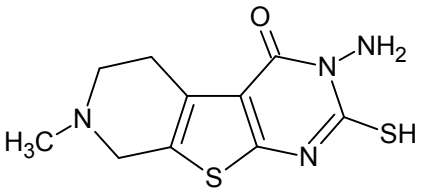
S. No.	R	Anti-inflammatory activity	
		in vitro	***in vivo***
a	(1)	34.22	33.40
b	2-Hydroxy	46.01	42.22
c	4-Hydroxy	42.31	42.00
d	2-Nitro	26.00	29.46

Cont…

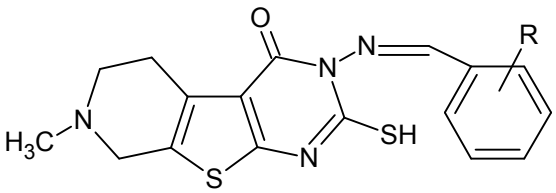
S. No.	R	Anti-inflammatory activity	
		in vitro	***in vivo***
e	3-Nitro	28.01	36.28
f	4-Nitro	31.08	36.48
g	4-Methoxy	24.84	36.10
h	3-Methoxy-4-hydroxy	28.27	35.17
i	2-Chloro	34.26	30.22
j	3, 4, 5-Trimethoxy	38.22	42.26
k	4-Dimethylamino	34.40	38.86
	Ibuprofen	70.01	76.02

Table 2

S. No.	R	Antibacterial activity			
		Gram positive		Gram negative	
		Staphylococcus aureus	***B. subtilis***	***E. coli***	***S. typhi***
a	(1)	24	20	22	28
b	2-Hydroxy	14	16	22	10
c	4-Hydroxy	16	12	20	11
d	2-Nitro	13	12	15	15
e	3-Nitro	14	14	16	15
f	4-Nitro	9	7	9	5
g	4-Methoxy	7	6	7	5
h	3-Methoxy-4-hydroxy	11	9	10	7
i	2-Chloro	9	13	6	9
j	3, 4, 5-trimethoxy	19	16	20	18
k	4-dimethylamino	11	10	10	10
	Ampicillin	21	4	4	24



(1)



Compounds

RESULTS AND DISCUSSION

The results of biological screening revealed that compound **b** show maximum anti-inflammatory activity in comparison with standard drug while compound **f** is active against Gram positive bacteria and compound **f** and **g** was found to active against Gram negative bacteria, but compound **g** shows maximum activity against both categories. However, starting compound was found to possess less activity than compound **a** to **j**. The presence of imino group contributes to antibacterial and anti-inflammatory activity, which is increased on substitution with phenyl group containing nitro group at para position (antibacterial activity) and hydroxyl group (anti-inflammatory activity)

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