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ANTI-INFLAMMATORY AND ANTIOXIDANT ACTIVITY OF SOME ACID CHLORIDE DERIVATIVES OF 2-AMINO-N-(3-CHLOROPHENYL)-5, 6-DIHYDRO-4H-CYCLOPENTA [b] THIOPHEN-3-CARBOXAMIDE

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ABSTRACT

2-Amino-N- (3-chlorophenyl)-5, 6-dihydro-4H-cyclopenta [b] thiophene-3-carboxamide was synthesized by application of Gewald reaction. The acid chloride derivatives were screened for *in vitro* anti-inflammatory and antioxidant activity comparable to that of ibuprofen and ascorbic acid, respectively.

Key words : Acid chloride derivatives, Thiophene, Anti-inflammatory activity, Antioxidant activity.

INTRODUCTION

Thiophene derivatives have attracted a great deal of interest owing to their medicinal activities. A wide spectrum of activities has been reported for these compounds, such as antimicrobial and antifungal[1-3], CNS depressant activity[4], sedative[5], antitumour[6], analgesic[7] and local anesthetic[8] activities. In our previous work, we reported the synthesis and antimicrobial activity of title compounds[9]. As part of this work, we report the anti-inflammatory and antioxidant activity of the title compounds.

EXPERIMENTAL

Anti-inflammatory screening

Screening of anti-inflammatory activity was carried out by inhibition of bovine serum albumin denaturation method[10] using ibuprofen as standard. The test compounds were dissolved in minimum amount of water and diluted with phosphate buffer (0.2M, pH

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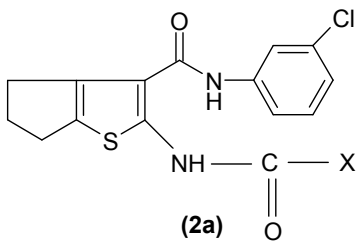
7.4). Test solutions of drug was mixed with albumin solution in phosphate buffer and incubated at $27^0 \pm 1^0$ C for 15 minutes. Denaturation was induced by keeping the reaction mixture at 60^0 C ± 1^0C in a water bath for 10 minutes. After cooling, the turbidity of the resulting solution was measured at 660 nm. Each experiment was done in triplicate and the average reading was taken. The results of biological screening are summarized in Table 1.

Antioxidant screening

Antioxidant activity was carried out by reduction method[11] where increase in absorbance of the reaction mixture indicates the reducing power of the samples. Test compounds were mixed with phosphate buffer and potassium ferricyanide [$K_3Fe(CN)_6$] (1%) and the mixture was incubated at 50^0C for 30 minutes. Then, trichloroacetic acid was added to mixture and the same was then centrifuged at 3000 rpm for 10 minutes. Finally, upper layer was separated, mixed with distilled water. Ferric chloride (0.1%) was added and the absorbance was recorded at 700 nm. Ascorbic acid was taken as standard for antioxidant activity. The results of biological screening are summarized in Table 1

Table 1. Anti-inflammatory and antioxidant activity



(2a)

Compound	X	Anti-inflammatory activity* (% Bovine serum inhibition)	Antioxidant activity (%)*
2a	Phenyl	28.32	15.61
2b	4-Aminophenyl	34.16	34.78
2c	2-Chlorophenyl	32.40	51.25
2d	4-Nitrophenyl	30.27	19.21
2e	3, 5-Dinitrophenyl	33.14	17.86

Cont…

Compound	X	Anti-inflammatory activity* (% Bovine serum inhibition)	Antioxidant activity (%)*
2f	3-Amino-5-bromophenyl	24.50	40.42
2g	2-Hydroxyphenyl	50.12	54.14
2h	2-Hydroxy-3, 5-dinitrophenyl	50.14	31.78
2i	4-Chlorophenyl	28.36	48.54
Ibuprofen	-	65.86	-
Ascorbic acid	-	-	98

*Results are average of three readings

RESULTS AND DISCUSSION

The results of anti-inflammatory and antioxidant revealed that compounds **2g** and **2h** show most potent anti-inflammatory activity. The compounds **2c**, **2g** and **2i** have show most potent anti-oxidant activity. The hydroxy substitution at ortho position made the compound to exhibit high anti-inflammatory and antioxidant activity. It indicates that the presence of electron releasing groups made the compounds to exhibit anti-inflammatory activity, while the presence of electron withdrawing groups made the compound to exhibit antioxidant activity comparable to that of standard drugs.

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