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**Der Pharma Chemica, 2013, 5(1):161-166**
*(http://derpharmachemica.com/archive.html)*

**ISSN 0975-413X**
**CODEN (USA): PCHHAX**

# Synthesis, characterization and biological studies of some novel piperidinothiophenes

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**ABSTRACT**

*In an attempt to find a new class of antimicrobial agents having anti-inflammatory activity, a series of thiophene containing Schiff base moiety were prepared via the reaction of ketone, 4-N-methyl piperidone with the isobutylcyanoacetamide using ammonium acetate/glacial acetic acid as an acidic catalyst with the arrangement of continuous removal of water followed by reacting starting compounds with substituted aryl aldehydes. These compounds were screened for their antibacterial activity against Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus), Gram-negative bacteria (Escherichia coli and Klebsiella pneumonia) and antifungal activity against (Aspergillus niger and Candida albicans) by using cup plate method. The results clearly revealed the potential antimicrobial and anti-inflammatory activity of all these piperidinothiophenes when compared with the standard drug Ampicillin and Ibuprofen. Structures of the newly synthesized compounds were established by elemental analysis and spectral data.*

**Key words:** fusedthiophene, piperidine, schiffs base, antibacterial, antifungal, anti- inflammatory activity.

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## INTRODUCTION

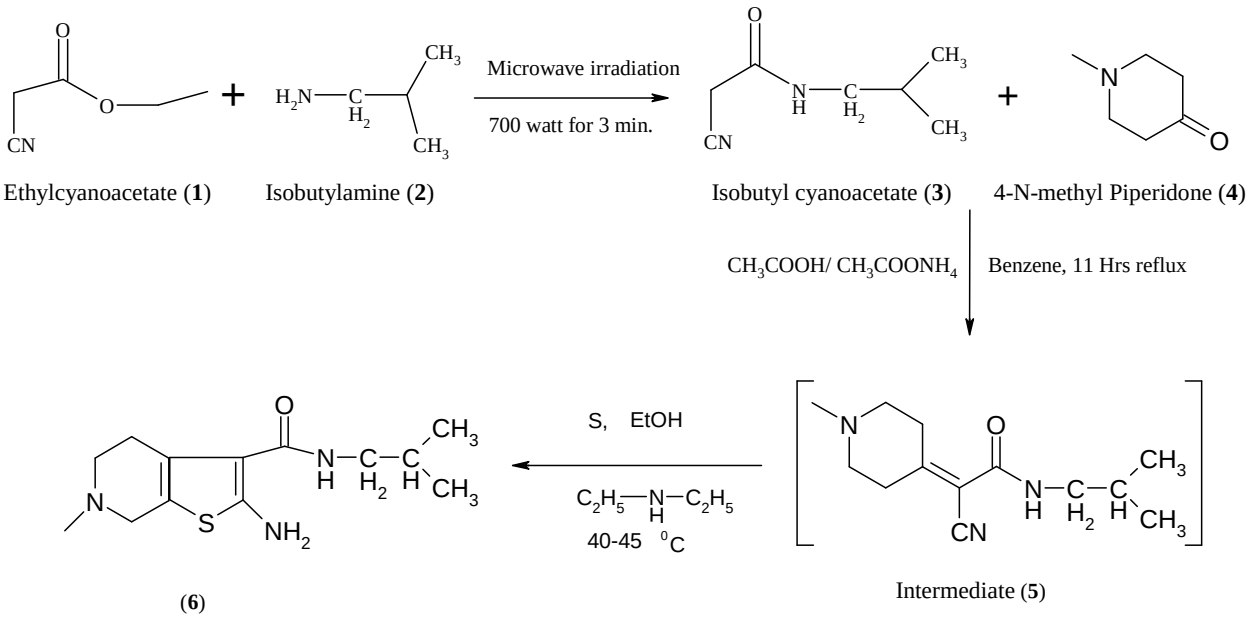
In continuation of our work on fused thiophenes[1-7], we report the synthesis of piperidinothiophenes. As it is well documented that fused thiophenes have large array of biological activities like anticancer[8], antitumor[8], anti-tubercular[9-10], antibacterial[11,1-6], and fungicidal[1-7] activities. They are also useful as antiparasitic[12], anti-inflammatory[13,14], analgesic[14-16] and MEK inhibitor[17], Antiarrhythmic[18], serotonin antagonist[18], antianxiety agents[18], Intestinal Calcium-Activated Chloride Channel inhibitor[19], and anticonvulsant activity[20]. On the other hand, careful literature survey revealed that piperidine and thiophene ring systems have occupied a unique position in the design and synthesis of novel biological active agents with remarkable analgesic and anti-inflammatory activities, in addition to their well documented potential antimicrobial activities. In view of the above-mentioned facts and in continuation of our interest in the synthesis of heterocycles containing thiophene moiety, to identify new candidates that may be value in designing new, potent, selective and less toxic antimicrobial agents having anti-inflammatory activity, we report herein the synthesis, antimicrobial and anti-inflammatory evaluation of some novel structure hybrids incorporating substituted phenyl moiety. The substitution pattern of phenyl ring was carefully selected so as to confer different electronic environment to the molecules.

## MATERIALS AND METHODS

All the melting points were determined in open capillaries, using Veego VMP- DS melting point apparatus, expressed in $^{o}$C and are uncorrected. All the chemicals used in the synthesis were obtained from standard commercial sources. Reactions were monitored by TLC using silica gel-G (S. D. Fine Chem. Pvt. Ltd, Mumbai,

India) as the adsorbent and the different solvent systems were used. The separations of the compounds were checked on TLC under UV lamp and also by Iodine Chamber.

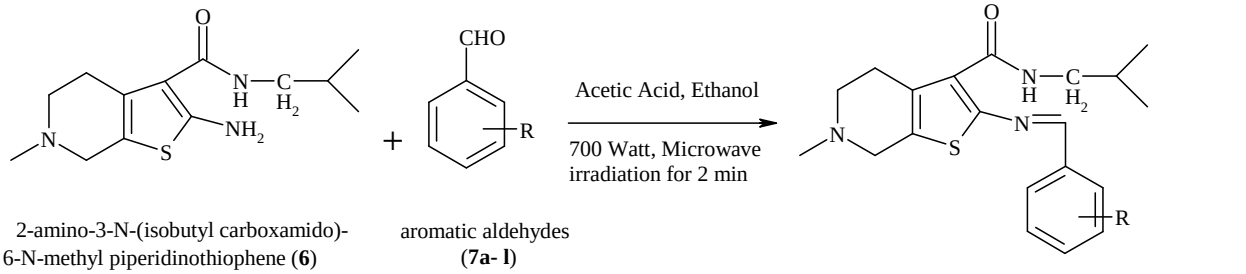
The $^1$H NMR spectra of the compounds were recorded either on HRMS (in $CDCl_3$/ $D_2O$) Bruker Avance 400 MHz (FTNMR) or Avance 300 MHz NMR spectrophotometer using TMS as an internal standard and the values are expressed in δ ppm. The infrared spectra were recorded on Perkin Elmer RX1 FTIR spectrophotometer. The mass spectra of the compounds were recorded on positive mode ESI- HRMS (m/ z) 100- 30000 Th model Agilent 6520 (Q- TOF) mass spectrophotometer. Bovine serum albumin (Merck Limited), Ibuprofen, Ampicillin and all other chemicals were of analytical grade.




Ethylcyanoacetate (**1**) Isobutylamine (**2**) Isobutyl cyanoacetate (**3**) 4-N-methyl Piperidone (**4**)

(**6**) Intermediate (**5**)

**Scheme 1**




2-amino-3-N-(isobutyl carboxamido)-6-N-methyl piperidinothiophene (**6**) aromatic aldehydes (**7a- l**)

2-[(substituted benzylidene)imino]-3-N-(isobutyl carboxamido)-6-N-methyl piperidinothiophene (**8**)

**Scheme 2**

**Synthesis of isobutylcyanoacetamide (3):**

A mixture of isobutylamine **2** (0.5 mole) and ethylcyano acetate **1** (0.5 mole) was taken in a conical flask and heated in microwave oven at 700 watt for 2-3 min. The reaction mixture was left at room temperature for overnight. The solid obtained was filtered, washed with water and dried. Recrystallization was done by ethanol: water mixture (5:1).

**Synthesis of 2-amino-3-N-(isobutyl carboxamido)-6-N-methyl piperidino thiophene (8):**

A mixture of isobutylcyanoacetamide **3** (0.04 mole), 4-N-methyl piperidone **4** (0.04 mole), ammonium acetate (1 g) and glacial acetic acid (2 mL) in benzene (80 mL) was refluxed with an arrangement for continuous separation of water involving dean stark apparatus. After 11 h. the reaction mixture was cooled, diluted with 10 mL benzene and washed with sodium carbonate solution (10% w/v in water) and water successively and dried over anhydrous sodium sulphate. The solvent was removed under vaccum and the intermediate crude product obtained was immediately processed for next the step.

To a mixture of 2-cyano-2-N-methylpiperilidene-N-isobutylacetamide **5** in alcohol (30 mL), was added sulphur (1.28 g; 0.04 mole) in portions followed by the addition of, diethyl amine (6.0 mL) drop wise with stirring. The reaction mixture was stirred for two and half hours at 40-45 ºC and chilled over night. The solid obtained was filtered, washed with ethanol and crystallized from isopropyl alcohol: water mixture (9:1).

**Synthesis of 2-[(substituted benzylidene) imino]-3-N-(isobutylcarboxamido)-6-N-methyl piperidinothiophenes (Schiff bases):**

A mixture of the starting compound **6** (0.005 mole) and the required aryl aldehydes **7** (substituted benzaldehydes, 0.005 mole) in ethanol (25 mL) and catalytic amount of glacial acetic acid was heated in microwave oven at 700 watt for 120 sec (2 min). The mixture was cooled to room temperature; the solid separated was filtered, washed with ethanol and crystallized from suitable solvent. By adopting the above synthetic procedure, compounds **8**a to **8**l were also synthesized. All these compounds were new and the characteristic physical and spectral data were presented separately in the tabular form.

**CHEMISTRY:**

1. 2-amino-3-isobutylcarboxamido-6-N-methyl piperidino thiophene **(81),** M.P.- 104$^0$C, I.R. (KBr, cm$^{-1}$) 3396 (N-H), 2928 (Ali-CH), 1625 (C=O), 780 (C-S), $^1$H NMR δ 8.85 (1H, s), 5.64 (2H, s), 3.44 (2H, s), 2.7 (2H, t), 2. 6 (2H, t), 2.5 (3H, s), 2.2 (2H, d), 1.5 (1H, m), 0.9 (6H, d), ESI- MS (M+1) 268. Anal. Calcd. for $C_{13}H_{21}N_3OS$: C 58.39,H 7.92,N 15.71,S 11.99. Found: C 58.33,H 7.90,N 15.72,S 11.99.

2. 2-[(4'-chloro benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8a),** M.P.- 198$^0$C, I.R. (KBr, cm$^{-1}$) 3185 (Aro-CH), 2928 (Ali-CH), 1630 (C=O), 1593 (C=N), 1085(Ar-Cl), 808 (C-N), 1541(Ar-C=C), 746 (C-S). $^1$H NMR δ 9.84 (1H, s), 8.95 (1H, s),7.7 (2H, d), 7.4 (2H, d), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.66 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92- 0.98 (6H, d), ESI- MS (M+1) 390. Anal. Calcd. for $C_{20}H_{24}ClN_3OS$: C 61.60,H 6.20,N 10.78,S 8.22. Found: C 61.59,H 6.20,N 10.79,S 8.20.

3. 2-[(4'-fluoro benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8b)**, M.P.- 187$^0$C, I.R. (KBr, cm$^{-1}$) 3322.5 (NH), 3123 (Aro-CH); 2935 (Ali-CH); 1629 (C=O), 1599 (C=N); 1230 (C-F), 825 (C-N), 749 (C-S). $^1$H NMR δ 10.05 (1H, s), 8.95 (1H, s),7.7 (2H, d), 7.2 (2H, d), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.9 (6H, d), ESI- MS (M+1) 374. Anal. Calcd. for $C_{20}H_{24}FN_3OS$: C 64.32,H 6.48,N 11.25,S 8.59. Found: C 64.33,H 6.47,N 11.28,S 8.57.

4. 2-[(4'-methyl benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8c),** M.P.- **202**$^0$C, I.R. (KBr, cm$^{-1}$) 3310 (NH), 3187 (Aro-CH), 2935 (Ali-CH), 1627 (C=O), 1535 (C=N), 833 (C-N), 779 (C-S). $^1$H NMR δ 9.91 (1H, s), 8.88 (1H, s),7.5 (2H, d), 6.8 (2H, d), 3.44 (2H, s), 2.92 (3H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 370. Anal. Calcd. for $C_{21}H_{27}N_3OS$: C 68.26,H 7.36,N 11.37,S 8.68. Found: C 68.24,H 7.34,N 11.38,S 8.68.

5. 2-[(4'-methoxy benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8d)** , M.P.-**173**$^0$C, I.R. (KBr, cm$^{-1}$) 3310 (NH), 3187 (Aro-CH), 2933 (Ali-CH), 1630 (C=O), 1545 C=N), 825 (C-N), 760 (C-S). $^1$H NMR δ 9.95 (1H, s), 8.95 (1H, s),7.3 (2H, d), 6.5 (2H, d), 3.36 (3H, s), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.50 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 386. Anal. Calcd. for $C_{21}H_{27}N_3O_2S$: C 65.42,H 7.06,N 10.90,S 8.32. Found: C 65.45,H 7.04,N 10.93,S 8.36.

6. 2-[(4'-hydroxy benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8e),** M.P.- **182**$^0$C, I.R. (KBr, cm$^{-1}$) 3456 (OH), 3112 (Aro-CH), 2935 (Ali-CH), 1653 (C=O), 1560 (C=N), 835 (C-N), 789 (C-S). $^1$H NMR δ 9.8 (1H, s), 8.6 (1H, s),7.3- 7.4 (2H, d), 6.6 (2H, d), 5.1 (1H, s), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.98 (6H, d), ESI- MS (M+1) 372. Anal. Calcd. for $C_{21}H_{27}N_3O_2S$: C 64.66,H 6.78,N 11.31,S 8.63. Found: C 64.63,H 6.76,N 11.32,S 8.64.

7. 2-(benzylidene imino-3-isobutylcarboxamido-6-N-methyl piperidino thiophene **(8f),** M.P.-**169**$^0$C, I.R. (KBr, cm$^{-1}$) 3115 (Aro-CH), 2926 (Ali-CH), 1651 (C=O), 1593 (C=N), 815 (C-N), 759 (C-S), 1562 (Ar-C=C). $^1$H NMR δ 9.98 (1H, s), 8.86 (1H, s),7.5- 7.6 (2H, d), 7.1- 7.4 (3H, m), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 356. Anal. Calcd. for $C_{20}H_{25}N_3OS$: C 67.57,H 7.09,N 11.82,S 9.02. Found: C 67.58,H 7.04,N 11.81,S 9.00.

8. 2-[(2'-chloro benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8g),** M.P.- **175**$^0$C, I.R. (KBr, cm$^{-1}$) 3184 (Aro-CH), 2935 (Ali-CH), 1645 (C=O), 1545 (C=N) , 1517 (Ar-C=C), 1080 (C-Cl) 815 (C-N), 755 (C-S). $^1$H NMR δ 9.84 (1H, s), 8.95 (1H, s),7.2- 7.6 (4H, m), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.66 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92- 0.97 (6H, d), ESI- MS (M+1) 390. Anal. Calcd. for $C_{20}H_{24}ClN_3OS$: C 61.60,H 6.20,N 10.78,S 8.22. Found: C 61.64,H 6.23,N 10.78,S 8.20.

9. 2-[(2'-fluoro benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8h),** M.P.- **180**$^0$C, I.R. (KBr, cm$^{-1}$) 3187 (Aro-CH), 2935 (Ali-CH), 1627 (C=O), 1535 (C=N), 1210 (C-F), 833 (C-N), 779 (C-S). $^1$H NMR δ 10.01 (1H, s), 8.97 (1H, s),7.0- 7.7 (4H, m), 3.46 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92-0.97 (6H, d), ESI- MS (M+1) 374. Anal. Calcd. for $C_{20}H_{24}FN_3OS$: C 64.32,H 6.48,N 11.25,S 8.59. Found: C 64.31,H 6.45,N 11.24,S 8.56.

10. 2-[(3',4'-dimethoxy benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8i),** M.P.- **198**$^0$C, I.R. (KBr, cm$^{-1}$) 3058 (Aro-CH), 2935 (Ali-CH), 1656 (C=O), 1539 (C=N), 825 (C-N), 771 (C-S), 1512 (Ar-C=C), 1276 (Ar-$OCH_3$). $^1$H NMR δ 9.92 (1H, s), 8.79 (1H, s),7.1 (1H, s), 6.9- 7.1 (2H, d), 3.72 (6H, s), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.50 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 416. Anal. Calcd. for $C_{22}H_{29}N_3O_3S$: C 63.59,H 7.03,N 10.11,S 7.72. Found: C 63.56,H 7.00,N 10.13,S 7.71.
11. 2-=[(3',4',5-trimetoxy benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8j),** M.P.- **203**$^0$C, I.R. (KBr, cm$^{-1}$) 3123(Aro-CH), 2935 (Ali-CH), 1629 (C=O), 1599 (C-N), 1510 Ar-C=C), 1276 ($OCH_3$), 825 (C-N), 789 (C-S). $^1$H NMR δ 9.9 (1H, s), 8.62 (1H, s), 6.6 (2H, d), 3.73 (9H, s), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.50 (3H, s), 2.22- 2.27 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 446. Anal. Calcd. for $C_{23}H_{31}N_3O_4S$: C 62.00,H 7.01,N 9.43,S 7.20. Found: C 62.01,H 7.00,N 9.42,S 7.16.
12. 2-[(3'-fluoro benzylidene)imino]-3- isobutylcarboxamido-6-N-methyl piperidino thiophene **(8k),** M.P.- **182**$^0$C, I.R. (KBr, cm$^{-1}$) 3176 (Aro-CH), 2916 (Ali-CH), 1692 (C=O), 1589 (C= N), 828 (C-N), 789(C-S), 1511 (Ar C=C), 1225 (C-F). $^1$H NMR δ 10.01 (1H, s), 8.9 (1H, s),7.5 (1H, d), 7.1- 7.4 (3H, m), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.9 (6H, d), ESI- MS (M+1) 374. Anal. Calcd. for $C_{20}H_{24}FN_3OS$,: C 64.32,H 6.48,N 11.25,S 8.59. Found: C64.31,H 6.44,N 11.24,S 8.57.
13. 2-[(2'-methyl benzylidene) imino]-3- isobutyl carboxamido-6-N-methyl piperidino thiophene **(8l),** M.P.- **194**$^0$C, I.R. (KBr, cm$^{-1}$) 3187 (Aro-CH), 2935 (Ali-CH), 1627 (C=O), 1535 (C=N), 833 (C-N), 779 (C-S). $^1$H NMR δ 9.89 (1H, s), 8.72 (1H, s), 7.1- 7.5 (4H, m), 3.44 (2H, s), 2.72- 2.77 (2H, t), 2.63- 2.67 (2H, t), 2.5 (3H, s), 2.38 (3H, s), 2.22- 2.28 (2H, d), 1.5 (1H, m), 0.92 – 0.97 (6H, d), ESI- MS (M+1) 370. Anal. Calcd. for $C_{21}H_{27}N_3OS$,: C 68.26,H 7.36,N 11.37,S 8.68. Found: C 68.22,H 7.34,N 11.36,S 8.64.

## BIOLOGICAL EVALUATION

### (i) Antibacterial Activity:

The antibacterial activity of synthesized thiophenes were conducted against two gram positive bacteria viz., *Bacillus subtilis* and *Staphylococcus aureus* and two gram negative bacteria viz., *Escherichia coli and Klebsiella pneumoniae* by using cup plate method. Ampicillin was employed as reference standards to compare the results.

### (ii) Antifungal Activity:

All those compounds screened for antibacterial activity were also tested for their antifungal activity. The fungi employed for screening were *Aspergillus niger* and *Candida albicans*. Miconazole was employed as standard to compare the results.

### (iii) Anti-Inflammatory Activity:

**Inhibition of bovine serum albumin denaturation[21] and anti- inflammatory activity:**

Clinically established anti-inflammatory drugs have shown to inhibit heat coagulation of proteins. These anti-inflammatory drugs have exerted an inhibitory activity on immune haemolysis and also have suppressive effect on vascular reactivity. Denaturation as one of the causes of inflammation is well documented. Anti-inflammatory drugs interact in some way with proteins. To gauge the interaction between the drug and the proteins, the stability of proteins against heat coagulation can be measure (Inhibition of bovine serum albumin denaturation).

**Table 1: Antibacterial activity of piperidinothiophenes (8a to 8l):**

| Compound | R | Zone of inhibition (mm) * | | | |
|---|---|---|---|---|---|
| | | *S.aureus* | *B.subtilis* | *E.coli* | *K. pneumoniae* |
| **8** | - | 08 | 06 | 05 | 07 |
| **8a** | 4- chloro | 17 | 14 | 12 | 14 |
| **8b** | 4- fluoro | 16 | 12 | 14 | 15 |
| **8c** | 4- methyl | 09 | 08 | 06 | 07 |
| **8d** | 4- methoxy | 12 | 07 | 06 | 06 |
| **8e** | 4- hydroxy | 13 | 05 | 07 | 08 |
| **8f** | H | 11 | 05 | 05 | 08 |
| **8g** | 2- chloro | 14 | 10 | 09 | 09 |
| **8h** | 2- fluoro | 14 | 11 | 09 | 10 |
| **8i** | 3,4- dimethoxy | 12 | 08 | 08 | 08 |
| **8j** | 3,4,5- trimethoxy | 12 | 08 | 07 | 08 |
| **8k** | 3- fluoro | 12 | 11 | 09 | 10 |
| **8l** | 2- methyl | 09 | 08 | 06 | 06 |
| **Ampicillin** | - | **19** | **16** | **14** | **17** |

The test compounds were dissolved in minimum amount of DMF and diluted with phosphate buffer (0.2 mole, pH 7.4). Final concentration of DMF in all solution was less than 2.5%. Test solution (1mL) containing different

concentrations of drug was mixed with 1 mL of 1 mmole albumin solution in phosphate buffer and incubated at $27^0 \pm 1^0$C for 15 min. Denaturation was induced by keeping the reaction mixture at $60^0 \pm 1^0$C in a water bath for 10 min. After cooling the turbidity was measured at 660 nm. Percentage inhibition of denaturation was calculated from control where no drug was added. Each experiment was done in triplicate and the average was taken. The percentage of inhibition is calculated from the following formula.

% Inhibition =100 (1-Vt/Vc)

**Table 2: Antifungal activity of piperidinothiophenes (8a to 8l):**

| Compound | R | Zone of inhibition (mm) * | |
|---|---|---|---|
| | | *Aspergillus niger* | *Candida albicans* |
| **8** | - | 12 | 09 |
| **8a** | 4- chloro | 24 | 22 |
| **8b** | 4- fluoro | 22 | 20 |
| **8c** | 4- methyl | 12 | 10 |
| **8d** | 4- methoxy | 14 | 10 |
| **8e** | 4- hydroxy | 12 | 12 |
| **8f** | H | 12 | 12 |
| **8g** | 2- chloro | 22 | 16 |
| **8h** | 2- fluoro | 20 | 18 |
| **8i** | 3,4- dimethoxy | 14 | 13 |
| **8j** | 3,4,5- trimethoxy | 15 | 13 |
| **8k** | 3- fluoro | 19 | 18 |
| **8l** | 2- methyl | 13 | 19 |
| **Miconazole nitrate** | - | **30** | **26** |

**Table 3: *In vitro* Anti-inflammatory activity data of piperidinothiophenes (8a to 8l):**

| Compound | R | Anti-inflammatory activity (% Bovine serum inhibition) |
|---|---|---|
| **8** | - | 38.10 |
| **8a** | 4- chloro | 39.25 |
| **8b** | 4- fluoro | 40.40 |
| **8c** | 4- methyl | 43.80 |
| **8d** | 4- methoxy | 56.38 |
| **8e** | 4- hydroxy | 52.42 |
| **8f** | H | 39.80 |
| **8g** | 2- chloro | 40.20 |
| **8h** | 2- fluoro | 40.40 |
| **8i** | 3,4- dimethoxy | 55.26 |
| **8j** | 3,4,5- trimethoxy | 58.28 |
| **8k** | 3- fluoro | 45.10 |
| **8l** | 2- methyl | 40.72 |
| **Ibuprofen** | -- | 68.55 |

## RESULTS AND DISCUSSION

**Antibacterial activity:**

The antibacterial activity of all the piperidinothiophenes synthesized has been evaluated by using cup plate method. The results of this activity are shown in Table 1. The results clearly revealed the potential antibacterial activity of all piperidinothiophenes, when compared with the standard drug ampicillin, but not at an identical dose level. Of all the compounds tested, compound 8a having the chloro group at the *para* position of the phenyl ring, showed maximum activity and this is followed by compounds 8b and 8g, having fluorine and chlorine substitution at *para* and *ortho* positions respectively. The rest of the compounds showed mild to moderate activity.

**Antifungal activity:**

The antifungal activity of the substituted thiophenes was evaluated against *A. niger* and *C. albicans*, employing miconazole nitrate as the standard drug using the cup-plate method. A close examination of the Table-2 pertaining to the antifungal activity data of piperidinoothiophenes revealed that all the compounds in this series have been found to be effective against *A. niger* but not against *C. albicans*, when compared with the reference standard. The antifungal activity of compounds with halogen substitution was found to be more than those with electron releasing substituents. Of all the compounds tested, 8a having chlorine substitution at *para* position showed the maximum activity followed by compounds 8b and 8g with fluoro and chloro groups at *para* and *ortho* position respectively.

**Anti- inflammatory activity:**

The results of anti-inflammatory activity were shown in Table 3. The results clearly revealed the potential anti-inflammatory activity of all these piperidinothiophenes when compared with the standard drug ibuprofen. Of all the compounds tested, compound 8j having trimethoxy substitutionat 3$^{rd}$, 4$^{th}$ and 5$^{th}$ position on the aromatic ring of thiophne showed maximum activity and this is followed by compounds 8d and 8i having a *para* hydroxyl and dimethoxy substituents at 3$^{rd}$ and 4$^{th}$ position on the phenyl ring. The results demonstrated the necessity of electron donating substituents on aromatic ring, as they enhanced the activity.

## REFERENCES

[1]. S. Srivastava, B. Das, Y. RajendraPrasad, *Int. J. Chem. Sci.*, **2012**, 10(4), 1999-2009.
[2]. S. Srivastava, B. Das, R. Shukla, Y. Rajendra Prasad, *Asian J. Pharm. Life Sci.*, **2012**, 2(2), 234-251.
[3]. S. Srivastava, B. Das, Y. Rajendra Prasad, *Der. Pharm. Let.*, **2012**, 4(4), 1214-1220.
[4]. S. Srivastava, B. Das, *Der. Pharm. Chem.*, **2011**, 3(6), 103-111.
[5]. S. Srivastava, B. Das, *Int. J. Chem. Sci.*, **2009**, 7(3), 1779-1783.
[6]. S. Srivastava, B. Das, M. Raghuprasad, S. Mohan, *Asian J Chem*, **2007**, 19(4), 2813-2817.
[7]. B. Das, S. Srivastava, J. Sarvanan, S. Mohan, *Asian J. Chem.*, **2007**, 19(5), 4118-20.
[8]. R. Romagnoli, P.G. Baraldi, C.L. Cara, E. Hamel, G. Basso, R. Bortolozzi, G. Viola, *Eur. J. Med. Chem.*, **2010**, 45, 5781-91
[9]. L. Xiaoyun, B. Wan, S.G. Franzblau, Q. You, *Eur. J. Med. Chem.*, **2011**, 46, 3551- 63.
[10]. K. Balamurugan, S. Perumal, A.S.K. Reddy, P. Yogeeswari, D. Sriram, *Tetra. Lett.*, **2009**, 50, 6191–95.
[11]. J.F.D. Chabert, B. Marquez, L. Neville, L. Joucla, S. Broussous, P. Bouhours, E. David, S.P. Rostaing, B. Marquet, N. Moreaub, M. Lemaire, *Bioorg. Med. Chem.*, **2007**, 15, 4482–97.
[12]. J.G. Gonzalez, C.E. Stephens, T. Wenzler, R. Brun, F.A. Tanious, W.D. Wilson, T. Barszcz, T.A. Werbovetz, D.W. Boykin, *Eur. J. Med. Chem.*, **2007**, 42, 552- 57.
[13]. A.M. Isloor, B. Kalluraya, K.S. Pai, *Eur. J. Med. Chem.*, **2010**, 45, 825–30.
[14]. I.M.I.Fakhr, M.A.A. Radwan, S. El-Batran, O.M.E.A El-Salam, S.M. El-Shenawy, *Eur. J. Med. Chem.*, **2009**, 44, 1718- 25.
[15]. D.W. Nelson, J.M. Frost, K.R. Tietje, A.S. Florjancic, K. Ryther, W.A. Carroll, M.J. Dart, A.V. Daza, B.A. Hooker, G.K. Grayson, F. Yihong, T.R. Garrison, O.F. El-Kouhen, B. Yao, M. Pai, P. Chandran, C. Zhu, C. Hsieh, M.D. Meyer, *Bioorg. Med. Chem. Let.*, **2012**, DOI, 10.1016/j.bmcl. 2012.01.121
[16]. C.E. Bennett, D.A. Burnett, W.J. Greenlee, C.E. Knutson, P. Korakas, C. Li, D. Tulshian, W. Wu, R. Bertorelli, S. Fredduzzi, M. Grilli, G. Lozza, A. Reggiani, A. Veltri, *Bioorg. Med. Chem. Lett.*, **2012**, 22, 1575–78.
[17]. V.E. Laing, D.C. Brookings, R.J. Carbery, J.G. Simorte, M.C. Hutchings , B.J. Langham, M.A. Lowe, R.A Allen, J.R. Fetterman, J. Turner, C. Meier , J. Kennedy, M. Merriman, *Bioorg. Med. Chem. Lett.*, **2012**, 22, 472–75.
[18]. A.G.E. Amra, M.H. Sherif, M.G. Assy, M.A. Al-Omar, I. Ragab, *Eur. J. Med. Chem.*, **2012**, 45, 5935- 42.
[19]. R.D.L. Fuente, W. Namkung, R. Mills, A.S.Verkman, *Mol. Pharm.*, **2008**, 73, 758–68.
[20]. A.S. Oganisyan, S. Noravyan, A. Dzhagatspanyan, G. Akopyan G., *Pharm. Chem. J.*, **2001,** 35, 127-9.
[21]. G. Elias, M.N.A. Rao, Indian J. Exp. Biol., **1988,** 26, 540-2.