*Oriental Journal of Chemistry* Vol. **25**(3), 511-514 (2009)

# Synthesis and pharmacological screening of dimethylaminophenyl substituted pyrimidinoimidazolinones

**R. PERUMAL[1], AKALANKA DEY[2*], R. MANAVALAN[2], KALYANI PRAKASAM[1], G.M. SREENIVASA[3] and E. JAYACHANDRAN[3]**

[1]V. V. Puram Institute of Pharmaceutical Science, Bangalor - 70 (India).
[2*] Dept. of Pharmacy, Annamalai University, Annamalai Nagar - 608 002 (India).

(Received: March 03, 2009; Accepted: April 13, 2009)

**ABSTRACT**

The various substituted pyrimidinoimidazolinones have been synthesized and evaluated for their antimicrobial activity. Structure of these products has been established by IR. 'HNMR data significant antimicrobial activity were observed for some members of the series.

**Key words:** Pyrimidine, Imidazole, Dimethylaminobenzene.

## INTRODUCTION

Pyrimidines, being an integral part of DNA and RNA imparts to diverse pharmacological properties as effective bactericide, fungicides[1-3] certain pyrimidine derivatives are also known to display antimalarial[4] antifilarial[5] and antileishmanial[6] activities. The biodynamic property of this ring system prompted up to design pyrimidine derivatives stimulating pharmacophore and substituents responsible for diverse pharmacological activities. Imidazolinones exhibit diverse biological properties[7]. Hence synthesis of new imidazolinones is of considerable interest. In the recent years the chemistry of Oxazolones has received much attentions due to their use as intermediate for the synthesis of some heterocyclic sytem[8]. Imidazolinones have been reported to possess antifungal[9], anti-inflammatory[10], anti viral and antihistaminic activity.

## MATERIAL AND METHODS

Melting points were determined by open capillary tube method and are uncorrected T. L. C. was run on silica gel G plates using Ethyl acetate, Butanol, Chloroform, (1:2:1) as developing solvents for the purity as the compounds. IR spectra were recorded on SHIMAZU FTIR- 89005 spectrophotometer, by using NUJOL MULL technique.

All the compounds synthesised were screened for antibacterial and antifungal activities of two different concentrations (50µg/ ml, 100 µg / ml) against staphylococcus aureus, *Bacillus subrillis Pseudomonas aureus and candida albicans, Asperagillus niger,* by cup plate method using procaine penicillin, streptomycin and Griseofulvin respectively as standards. Compounds showed considerable activity agaisnt all species tested at 50 µg/ml and 100 µg/ml. the substituted compounds IVa, IVb, IVe, IVf, IVg, IVh, IVl, IVm, IVn, showed promising activity against C. *albicans and Aspergillus niger*. The remaining compounds showed mild and moderate activity. The compounds IVa, IVc, IVf, IVg, IVh, IVm, IVn, IVb, IVh, IVl, IVn, have prominent antimicrobial activity against *Bacillus subrillis and Pseudomonas aureus* respectively. (Table 2 3).

**Preparation of 6-Dimethylaminophenyl-5-cryano-2-mercapto-3, 4-dihydro pyrimidin-4-one**

Mixture of ethylcyanoacetate (50m moles) thiourea (50m moles) Dimethylamino benzaldehyde (50m moles) potassium carbonate (50m moles) in

absolute ethanol (50ml) was refluxed for 12 hrs. then neutralised with glacial acetic acid. The product was isolated and crystallised from aq. ethanol CN group at 2205 $cm^{-1}$, pyrimidine carbonyl group at 1685 $cm^{-1}$, aromatic C=C at 1610 $cm^{-1}$.

**Preparation of 6-Dimethylaminophenyl-5-cyano-2-methyl thio-3-N-methyl-3,4-dihydropyrimidin-4-one**

The above synthesized product (10m moles) in DMF (20ml) potassium carbonate (20m moles) and Methyl iodide (20m moles) were added and stirred for 3hrs. Then reaction mixture was diluted with cold water and neutralized by glacial acetic acid. The product was crystallized from dioxam.

CN group, 1617$cm^{-1}$, for pyrimidine carboxyl, C=N-1542$cm^{-1}$, 2820-2762$cm^{-1}$ for N-methyl and 1330$cm^{-1}$ for S-methyl groups.

**Preparation of 6-Dimethylaminophenyl-5-cyano-2-hydrazino-3-N-methyl-3-, 4-dihydropyrimidin-4-one**

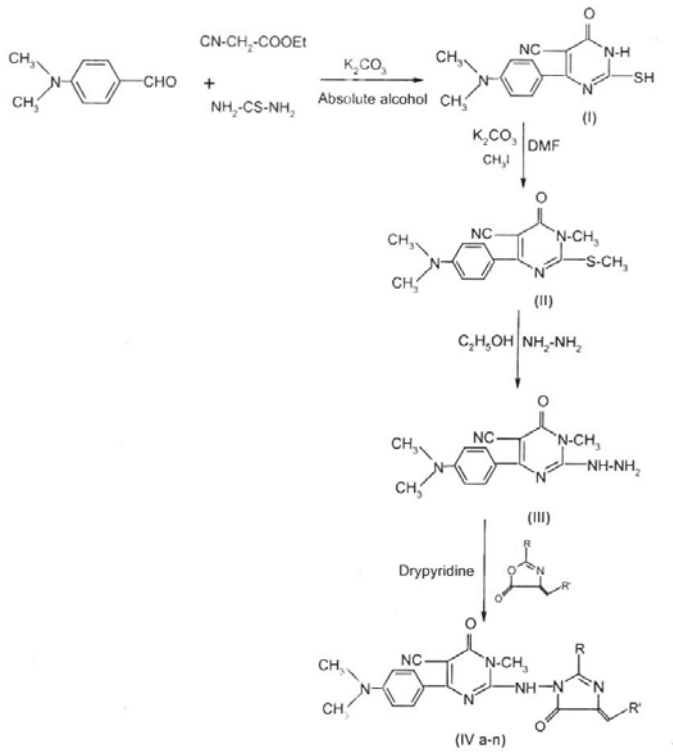
The said above compound II(10m moles) and hydrazine hydrate (30m moles) in absolute ethanol was refluxed for 10hrs. Then the reaction mixture was poured into ice, the product was crystallized by DMF.

-NH-$NH_2$ stretching at 3425$cm^{-1}$, CN group at 2300$cm^{-1}$, 909 $cm^{-1}$ to 666 $cm^{-1}$ due to primary amino wagging.

**General procedure for preparation of Dimethylaminophenyl substituted pyrimidinoimidazolinones[7-8]**

The mixture of III (0.005 mol) and separately prepared azalactones of aromatic, substituted aromatic, heterocyclic aldehyde (0.005 mol) was refluxed in presence of dry pyridine, for 6hrs. then the reactant mass were poured into the crushed ice and acidified with dilute hydrochloric acid, the product was crystallized by suitable solvent.

255$cm^{-1}$ due to CN group, 1675$cm^{-1}$ and 1700$cm^{-1}$ due to pyrimidine and imidazolinone ring 1600$cm^{-1}$ and 1410$cm^{-1}$ C=C, and C=N of the aromatic ring system.




**Scheme 1**

## RESULTS AND DISCUSSION

### Antibacterial activity

Dimethylaminophenyl substituted pyrimidinoimidazolinones series was tested for antibacterial activity. To highest antibacterial activity, activity index were calculated which were calculated which is defined in table. The compound showing activity Index more than 0.7 were considered to be significantly active. Compounds IVa, IVb, IVf, IVh, IVi, IVl, IVm, IVn at 50µg/ml and 100 µg/ml concentration were significantly active against

**Table 1: Analytical Data**

| S. No. | Compound code | % Yield | Melting Point | Mol. Formula | % Calculated M. Wt | C | H | N |
|---|---|---|---|---|---|---|---|---|
| 1 | IV a | 60 | 107 | $C_{30}H_{25}O_2N_7$ | 515 | 69.90 | 4.85 | 19.03 |
| 2 | IV b | 68 | 147 | $C_{30}H_{25}O_2N_7Cl$ | 549.5 | 65.51 | 4.37 | 17.83 |
| 3 | IV c | 67 | 152 | $C_{30}H_{25}O_4N_8$ | 560 | 64.29 | 4.29 | 20.00 |
| 4 | IV d | 59 | 112 | $C_{31}H_{25}O_4N_7$ | 559 | 66.55 | 4.83 | 17.53 |
| 5 | IV e | 70 | 109 | $C_{31}H_{27}O_3N_7$ | 535 | 69.53 | 5.05 | 18.32 |
| 6 | IV f | 67 | 107 | $C_{32}H_{29}O_2N_8$ | 552 | 69.57 | 5.25 | 20.29 |
| 7 | IV g | 59 | 179 | $C_{30}H_{25}O_3N_7$ | 531 | 67.80 | 4.71 | 18.45 |
| 8 | IV h | 67 | 144 | $C_{32}H_{27}O_2N_7$ | 541 | 70.98 | 4.99 | 18.12 |
| 9 | IV i | 74 | 179 | $C_{28}H_{23}O_3N_7$ | 505 | 66.53 | 4.55 | 19.41 |
| 10 | IV j | 74 | 116 | $C_{25}H_{23}O_2N_7$ | 453 | 66.23 | 5.07 | 21.63 |
| 11 | IV k | 75 | 162 | $C_{25}H_{22}O_2N_7Cl$ | 487.5 | 61.54 | 4.52 | 20.10 |
| 12 | IV l | 70 | 152 | $C_{25}H_{22}O_4N_8$ | 498 | 60.24 | 4.42 | 22.49 |
| 13 | IV m | 71 | 129 | $C_{26}H_{25}O_4N_7$ | 499 | 62.53 | 5.01 | 19.64 |
| 14 | IV n | 82 | 134 | $C_{26}H_{25}O_3N_7$ | 483 | 64.06 | 5.18 | 20.29 |

**Table 2: Antibacterial activity**

| S. No. | Name of the compounds | Mean zone of inhibition (in mm)* | | | |
|---|---|---|---|---|---|
| | | *Bacillus subtillis* | | *Pseudomonas aureus* | |
| | | 50µg | 100µg | 50µg | 100µg |
| 1 | Procaine penicillin | 21 | 25 | - | - |
| 2 | Streptomycin | - | - | 20 | 23 |
| 3 | IV a | 15 (0.71) | 19 (0.76) | 15 (0.75) | 19 (0.82) |
| 4 | IV b | 15 (0.71) | 18 (0.72) | 16 (0.80) | 21 (0.91) |
| 5 | IV c | 16 (0.76) | 17 (0.68) | 14 (0.7) | 17 (0.73) |
| 6 | IV d | 13 (0.61) | 16 (0.64) | 15 (0.75) | 19 (0.82) |
| 7 | IV e | 14 (0.66) | 17 (0.68) | 14 (0.7) | 18 (0.78) |
| 8 | IV f | 15 (0.71) | 19 (0.76) | 15 (0.75) | 19 (0.82) |
| 9 | IV g | 16 (0.76) | 18 (0.72) | 15 (0.75) | 19 (0.82) |
| 10 | IV h | 17 (0.81) | 17 (0.68) | 16 (0.8) | 21 (0.91) |
| 11 | IV i | 15 (0.71) | 16 (0.64) | 16 (0.8) | 21 (0.91) |
| 12 | IV j | 12 (0.56) | 16 (0.64) | 15 (0.75) | 19 (0.82) |
| 13 | IV k | 14 (0.66) | 17 (0.68) | 14 (0.7) | 18 (0.78) |
| 14 | IV l | 15 (0.71) | 18 (0.72) | 15 (0.75) | 20 (0.86) |
| 15 | IV m | 14 (0.66) | 19 (0.76) | 14 (0.7) | 19 (0.82) |
| 16 | IV n | 11 (0.51) | 20 (0.8) | 15 (0.75) | 20 (0.86) |

*Bacillus subrillis* (Gram +ve) and *pseudomonas aureus* )Gram –ve).

**Antifungal Activities**

Dimethylaminophenyl substituted pyrimidinoimidazolinones series was tested for antifungal activity. To highest antifungal activity, activity index were calculated which were calculated which is define in table. The compound showing activity index more than 0.7 were considered to be significantly active. Compounds IVe, IVf, IVi, IVm, IVn, at 50µg/ml and 100µg/ml concentration were significantly active against C.*albicans and A.niger.*

**ACKNOWLEDGEMENTS**

The authors are thankful to The Principal VIPS and the Vokkaliga sangha Management President, General Secretary. Directors, and Dept. of Pharmacy, Annamalai University, Annamalai Nagar for providing the opportunity to carry out this research work.

**Table 3: Antibacterial activity**

| S. No. | Name of the compounds | Mean zone of inhibition (in mm)* | | | |
|---|---|---|---|---|---|
| | | *Candida albicans* | | *Aspergillus niger* | |
| | | 50µg | 100µg | 50µg | 100µg |
| 1 | Griseofulvin | 21 | 25 | 21 | 25 |
| 2 | IV a | 11 (0.51) | 15 (0.60) | 14 (0.66) | 19 (0.76) |
| 3 | IV b | 13 (0.61) | 16 (0.64) | 14 (0.66) | 18 (0.72) |
| 4 | IV c | 12 (0.56) | 16 (0.64) | 13 (0.61) | 18 (0.72) |
| 5 | IV d | 12 (0.56) | 16 (0.64) | 12 (0.57) | 15 (0.6) |
| 6 | IV e | 13 (0.61) | 18 (0.72) | 13 (0.61) | 18 (0.72) |
| 7 | IV f | 12 (0.56) | 16 (0.64) | 14 (0.66) | 20 (0.80) |
| 8 | IV g | 13 (0.61) | 16 (0.64) | 13 (0.61) | 19 (0.76) |
| 9 | IV h | 12 (0.56) | 15 (0.6) | 14 (0.66) | 19 (0.76) |
| 10 | IV i | 12 (0.56) | 16 (0.64) | 15 (0.71) | 20 (0.80) |
| 11 | IV j | 12 (0.56) | 15 (0.6) | 14 (0.66) | 19 (0.76) |
| 12 | IV k | 12 (0.56) | 16 (0.64) | 12 (0.57) | 16 (0.65) |
| 13 | IV l | 12 (0.56) | 16 (0.64) | 14 (0.66) | 19 (0.76) |
| 14 | IV m | 13 (0.61) | 18 (0.74) | 14 (0.66) | 20 (0.8) |
| 15 | IV n | 13 (0.61) | 18 (0.72) | 12 (0.57) | 16 (0.65) |

**REFERENCES**

1. J. M. Parmar, J. J. Modha and A. R. Parikh, *Indian J. Chem.,* **38B**: 440-444 (1999).
2. A. I. Vogel, *Text book of Practical organic chemistry*, ELBS, 4th edition, 884-85 (1978).
3. Sankyo Co, Ltd., Ube Industries Ltd.; Japan Kokai Tokyo Koho JP 5936, 667 [8436, 677].
4. Falco E. A., *Brit J. Pharmacol*, **6**:185 (1961).
5. Howells R. E., Tinsly J., Devaney E. and Smith G., *Acta Tropica,* **38**: 289 (1982); *Chem. Abstr.,* **96**: 384K (1982).
6. S.K. Nandeeshaiah & Sarvottam Y. Ambekar, *Indian J. Chem.*, **37B**: 995-1000 (1998).
7. Mazur I. A., Sinyak R. S., Mandrichenko B. Y. and Stoyanovich S. S., *Farm. Zh. Kiew)*, **1**: 56 (1987).
8. El-Magharaby A., Bou El-Ela A., Khalafalla A. K. and E-El Shawi, *J. Indian Chem. Soc.,* **62**: 676 (1995).
9. Paney V.K. and Tandon Meenal, *I. J. Chem.,* **40B**: 527 (2001).
10. Sethna S. M. and Shah R. C., *J. Indian Chom. Soc.,* 1949 (1993).