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Synthesis and pharmacological screening of furfuryl substituted pyrimidinoimidazolinones

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ABSTRACT

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

Key words: Pyrimidine, Imidazole, Furan.

INTRODUCTION

Pyrimidines, being an integral part of DNA & RNA imparts to diverse pharmacological properties as effective bactericide, fungicides[1-3] certain pyrimidine derivatives are also known to display antimalarial[4] antifilarial[5] & antileishmanial[6] activities. The biodynamic property of this ring system prompted up to design pyrimidine derivatives stimulating pharmacophore & 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 attention due to their use as intermediate for the synthesis of some hetereocyclic system[8]. Imidazolinones have been reported to possess antifungal[9], antiinflammatory[10], anti viral and antihistaminic activity.

MATERIAL AND METHODS

Melting points were determined by open capillary tube method & 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 SHIMADZU FTIR – 89005 spectrophotometer, by using NUJOL MULL technique.

All the compounds synthesised were screened for antibacterial & antifungal activities of two different concentrations (50µg / ml, 100 µg / ml) against staphylococcus aureus, *Escherichia coil & candida albicans, Asperagillus flavus*, by cup plate method using procaine penicillin, streptomycin & Griseofulvin respectively as standards. Compounds showed considerable activity against all species tested at 50µg/ml & 100µg/ml. the substituted. Compounds showed promising activity against C. albicans & the compounds IVP_1, IVP_2, IVP_5, IVP_6, IVP_7, IVP_{10}, IVP_{13}. The remaining compounds showed mild & moderate activity. The compounds IVP_1, IVP_6, IVP_8, IVP_{11}, have prominent antimicrobial activity against *E.Coil & S.aureus* respectively. (Table 2&3).

Preparation of 6-Furfuryl-5-cyano-2-mercapto-3, 4-dihydro pyrimidin-4-one

Mixture of ethylcyanoacetate (50m moles) thiourea (50m moles) Furfuraldehyde (50m moles) potassium carbonate (50m moles) in absolute

ethanol (50ml) was refluxed for 12hrs then neutralized with glacial acetic acid. The product was isolated & crystallized from aq. ethanol CN group at 2200cm^{-1}, pyrimidine carbonyl group at 1680 cm^{-1}, aromatic C=C at 1600cm^{-1},

Preparation of 6-Furfural-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) & Methyl iodide (20m moles) were added & stirred for 3hrs. Then reaction mixture was diluted

Table 1: Analytical Data

S No.	Compound code	Yield (%)	m.p. (°C)	Molecular Formula	Molecular Wt	% Calculated C	H	N
1.	IV P_1	58	108	$C_{26}H_{18}O_3N_6$	462	67.53	3.89	18.18
2.	IV P_2	65	149	$C_{26}H_{17}O_3N_6Cl$	495.5	62.90	3.40	16.90
3.	IV P_3	63	150	$C_{26}H_{17}O_5N_7$	507	61.53	3.35	19.32
4.	IV P_4	60	115	$C_{27}H_{20}O_5N_6$	508	63.77	3.90	16.53
5.	IV P_5	74	112	$C_{27}H_{20}O_4N_6$	492	65.80	4.06	17.07
6.	IV P_6	64	105	$C_{28}H_{23}O_3N_7$	505	66.53	4.50	19.40
7.	IV P_7	60	183	$C_{26}H_{18}O_4N_6$	478	65.20	3.70	17.50
8.	IV P_8	62	146	$C_{28}H_{20}O_3N_6$	488	68.85	4.09	17.20
9.	IV P_9	72	185	$C_{24}H_{16}O_4N_6$	452	63.70	3.53	18.58
10.	IV P_{10}	74	114	$C_{21}H_{16}O_3N_6$	400	63.00	4.00	21.00
11.	IV P_{11}	73	159	$C_{20}H_{15}O_3N_6Cl$	421.5	56.93	3.50	19.92
12.	IV P_{12}	68	150	$C_{21}H_{15}O_5N_7$	445	56.62	3.30	22.00
13.	IV P_{13}	70	127	$C_{22}H_{18}O_5N_6$	446	59.10	4.00	18.80
14.	IV P_{14}	79	136	$C_{22}H_{18}O_4N_6$	430	61.30	4.10	19.50

Table 2: Antibacterial activity

S. No.	Compound code	*Mean zone of inhibition (in mm)*			
		Staphylococcus aureus		*Escherichia coli*	
		50 µg	100 µg	50 µg	100 µg
1.	Procaine penicillin	20	24	-	-
2.	Streptomycin	-	-	20	24
3.	IV P_1	07(0.35)	10(0.41)	06(0.30)	08(0.33)
4.	IV P_2	06(0.30)	08(0.33)	07(0.35)	08(0.33)
5.	IV P_3	06(0.30)	08(0.33)	06(0.30)	11(0.45)
6.	IV P_4	05(0.25)	07(0.29)	06(0.30)	09(0.37)
7.	IV P_5	06(0.30)	07(0.29)	05(0.25)	07(0.29)
8.	IV P_6	09(0.45)	11(0.45)	05(0.25)	09(0.37)
9.	IV P_7	08(0.40)	13(0.54)	05(0.25)	07(0.29)
10.	IV P_8	12(0.60)	15(0.62)	08(0.40)	12(0.50)
11.	IV P_9	07(0.35)	12(0.50)	08(0.40)	14(0.58)
12.	IV P_{10}	06(0.30)	08(0.33)	06(0.30)	08(0.33)
13.	IV P_{11}	09(0.45)	10(0.41)	05(0.25)	15(0.62)
14.	IV P_{12}	07(0.35)	08(0.33)	06(0.30)	08(0.33)
15.	IV P_{13}	06(0.30)	07(0.29)	06(0.30)	07(0.29)
16.	IV P_{14}	07(0.35)	09(0.37)	06(0.30)	07(0.29)

with cold water & neutralized by glacial acetic acid. The product was crystallized from dioxan.

CN group, 1617cm^{-1}, for pyrimidine carboxyl, C=N-1542cm^{-1}, 2820-2760cm^{-1} for N-methyl & 1330cm^{-1} for S-methyl groups.

Preparation of 6-Furfuryl-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 3425cm^{-1} , CN group at 2300 cm^{-1},909 cm^{-1} to 666 cm^{-1} due to primary amino wagging.

General procedure for preparation of Furfuryl substituted pyrimidinoimidazolinones[7-8].

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

2250cm^{-1}due to CN group, 1675cm^{-1} & 1700cm^{-1} due to pyrimidine & imidazolinone ring 1600cm^{-1} & 1400cm^{-1} C=C, & C=N of the aromatic ring system.

RESULTS AND DISCUSSION

Antibacterial activity

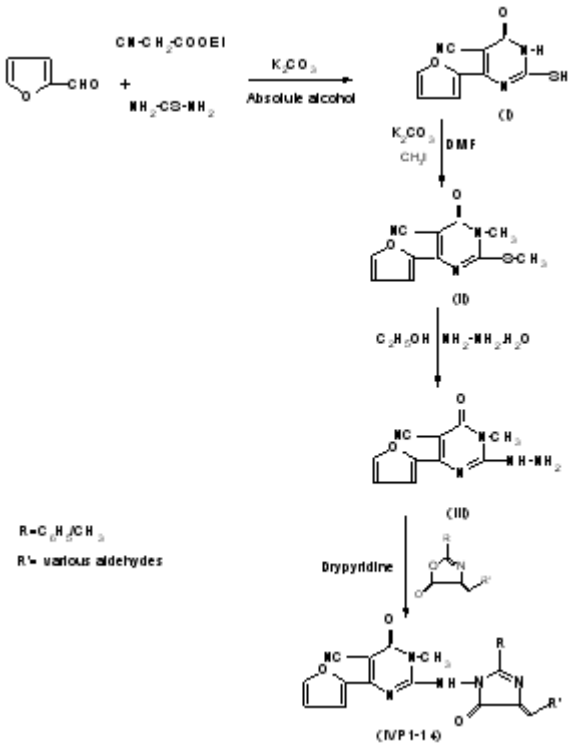
Furfuryl substituted pyrimidinoimid azolinones series was tested for antibacterial activity. To highest antibacterial activity, activity index were calculated which were calculated which is defined in table. The compound showing activity Index more than 0.7 were considered to be significantly active. Compounds IVP$_1$, IVP$_6$, IVP$_8$, IVP$_{11}$, at 50µg /ml and 100 µg/ml concentrations were significantly active against *S. aureus* (Gram+ve) and *E.Coli* (Gram-ve).

Antifungal activities

Furfuryl substituted pyrimidinoimida zolinones series was tested for antifungal activity. To highest antifungal activity, activity index were

Table 3: Antifungal activity

S. No.	Name of the compound	Mean zone of inhibition (in mm)			
		Candida albicans		*Asperagillus flavus*	
		50 µg	100 µg	50 µg	100 µg
1.	Griseofulvin	21	24	21	24
2.	IV P$_1$	13 (0.6)	17 (0.70)	19 (0.90)	22 (0.91)
3.	IV P$_2$	13 (0.6)	15 (0.62)	13 (0.6)	17 (0.70)
4.	IV P$_3$	11(0.52)	15 (0.62)	16 (0.76)	19 (0.79)
5.	IV P$_4$	13 (0.6)	17 (0.70)	09 (0.42)	12 (0.50)
6.	IV P$_5$	12 (0.57)	15 (0.62)	14 (0.66)	21 (0.87)
7.	IV P$_6$	12 (0.57)	13(0.54)	17 (0.8)	20 (0.83)
8.	IV P$_7$	16 (0.76)	20 (0.83)	17 (0.8)	21 (0.87)
9.	IV P$_8$	12 (0.57)	17 (0.70)	11 (0.52)	18 (0.75)
10.	IV P$_9$	10 (0.47)	16 (0.66)	12 (0.57)	15 (0.62)
11.	IV P$_{10}$	14 (0.66)	19 (0.79)	19 (0.90)	22 (0.91)
12.	IV P$_{11}$	11(0.52)	13(0.54)	10 (0.47)	12 (0.50)
13.	IV P$_{12}$	12(0.57)	13 (0.54)	16(0.76)	21 (0.87)
14 .	IV P$_{13}$	12(0.57)	13 (0.54)	20 (0.95)	23 (0.95)
15.	IV P$_{14}$	10 (O.47)	17 (0.70)	17 (0.8)	20 (0.83)



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 IVP_1, IVP_2, IVP_5, IVP_6, IVP_7, IVP_{10}, IVP_{13} at 50µg/ml and 100µg/ml concentration were significantly active against *C. albicans* and *A. flavus*

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REFERENCES

1. J.M. Parmar, J.J. Modha and A.R. Parikh, *Indian J. Chem* **38**B: 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 & Smith G, Acta Tropica, 38, 1982, 289; *Chem Abstr,* 96, 384k (1982).
6. S.K. Nandeeshaiah and Sarvottam Y. Ambekar, *Indian J.Chem* **37** B: 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., Abou El-Ela A., Khalafalla A.K. and E-El Shawi, *J. IndianChem. Soc.,* **62**: 676 (195).
9. Paney V.K. and Tandon Meenal *I.J. Chem.,* **40**B: 527 (2001).
10. Sethna S.M. and Shah R.C., *J. Indian Chom. Soc.,* 1949 (1993).