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SYNTHESIS OF SOME NOVEL PYRIMIDINONE AND PYRIMIDINE DERIVATIVES AND THEIR ANTIMICROBIAL ACTIVITY

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Abstract: Pyrimidinone are well named for their anticancer and antibacterial activities. Modern research is in search of lead compound that fights against Lymphoma and Malignant tumour. Some significant results are archived from the drugs having Pyrimidinone and Pyrimidine derivatives.

Keywords: Synthesis, heterocyclic chalcone derivatives, Anti cancer, Pyrimidinone derivatives

INTRODUCTION

It has been observed that there are certain tumour populations that seem to be heterogeneous in nature by the time the cancerous tumor is discovered after the usual biopsy examination**.** Whereas a few of the cells being resistant to some antineoplastic agents right at the very outset of the recommended treatment. The said findings hold good for certain well-established organs of the human body, such as colon, jejunal, adrenal, kidney and liver carcinomas.

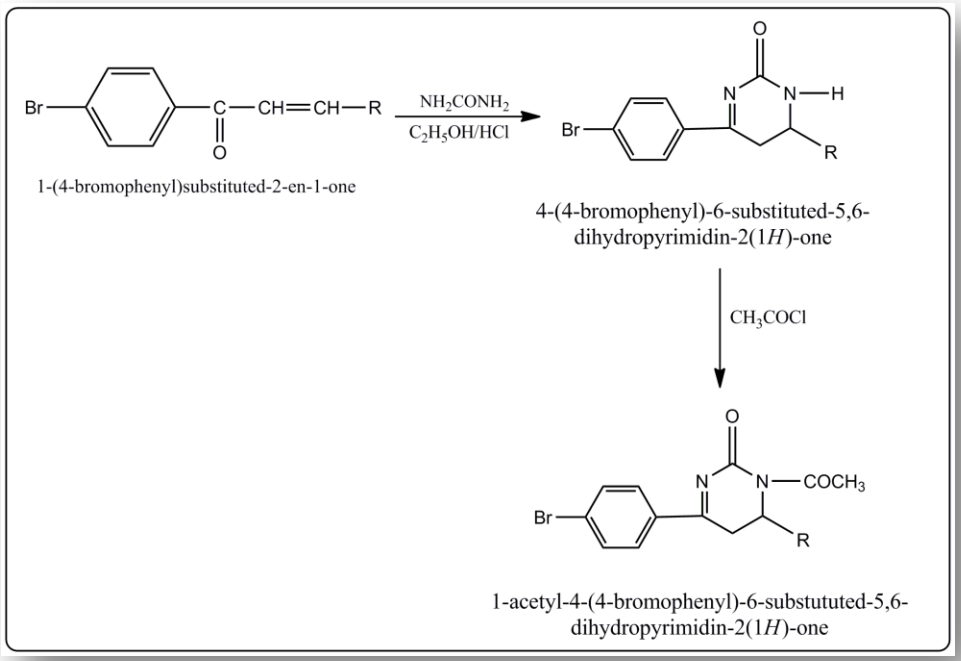
Rajarshi, reviewed the chemistry of Pyrimidinone, which have been studied extensively for their biodynamic behavior (I-IV) and industrial applications (V-VII).

Pyrimidinone derivatives and studied their antiproliferative activity in human ovarian adenocarcinoma cells, human lung carcinoma cells, and murine leukemia cells. Four of these substances were selected because of their higher antiproliferative activity.

The analysis of the cell cycle showed that all the selected compounds cause a partial G2/M block and the formation of polyploid cells.

Pyrimidinone compounds were tested for their interaction with the microtubular and tubulin was able to significantly bind dimers of α- and β-tubulin, probably causing a molecular distortion resulting in the disassembly of microtubules.

REACTION SCHEME



Where R = (a) Phenyl (b) 4-hydroxphenyl (c) 4-chlorophenyl (d) 4-hydrox-3-methoxyphenyl (e) 4-N,N-dimethylaminophenyl (f) 4-methoxyphenyl (g) 2-hydroxyphenyl (h) 4-methylphenyl (i) 3,4,5-triimethoxyphenyl (j) 3- phenoxyphenyl.

MATERIALS AND METHODS

(a) Preparation of 4-(4-bromophenyl)-6-substituted-5,6-dihydropyrimidin-2(1H)- one

A mixture of 4'-bromochalcone (2.33 g, 0. 01 mol), urea (0.60 g, 0.01 mol), concentrated hydrochloric acid (22 ml) and ethanol (95%, 30 ml) was refluxed on water-bath at 70-80 ^{o}C for 12 hours. The reaction mixture was then filtered while hot and allowed to cool at room temperature. This solution was then neutralized with 3N- sodium hydroxide. The resulting solid was filtered, washed with water and crystallized from ethanol (95%), light brown crystals obtained.

(b) Preparation of 1-acetyl-4-(4-bromophenyl)-6-substututed-5,6-dihydro - -pyrimidin-2(1H)-one

Take the brown crystals of 4-(4-bromophenyl)-6-substituted-5,6-dihydropyrimidin-2(1H)-one (2.56 gm,0.01 mol), acetyl chloride (8.0 ml) was added. The mixture was heated under reflux on water-bath at 35-40 ^{o}C for 2 hours. Evaporate excesss acetyl chloride and the oil remains was treated with ether. Crystallization of the product was carried out from benzene.

RESULTS AND DISCUSSION

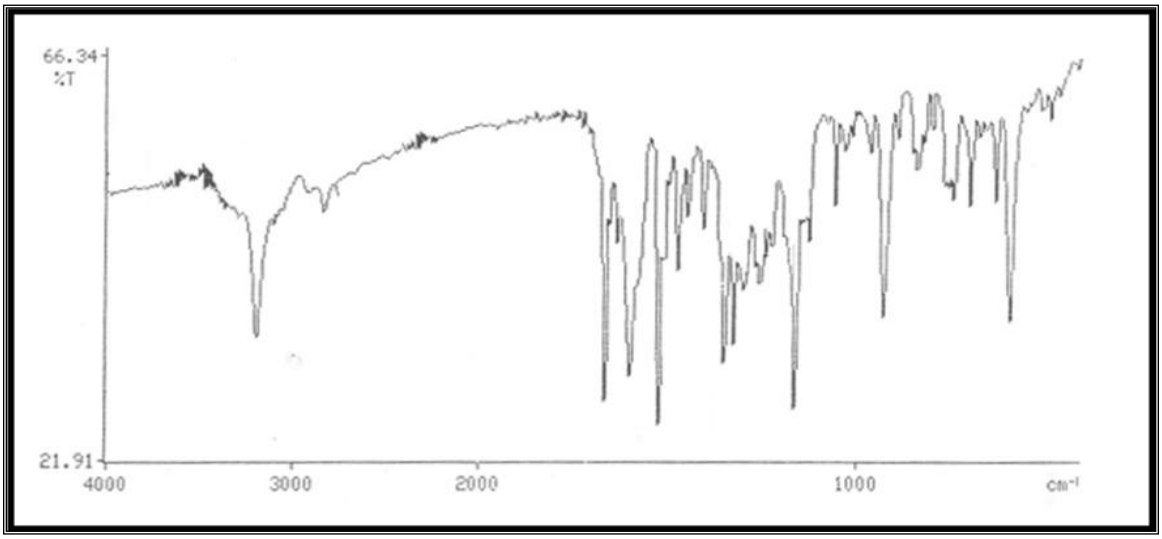
Physical and analytical data of compounds

No.	Code No.	R	Yield (%)	M.P. ^{o}C	C %	H %	N %
					Found		
1	a	Phenyl	89	190	53.70	3.75	12.27
2	b	4-hydroxphenyl	86	195	52.02	3.951	12.72
3	c	4-chlorophenyl	85	193	56.21	3.85	12.80
4	d	4-hydrox-3-methoxyphenyl	85	204	59.20	3.76	12.90
5	e	4-N,N-dimethylaminophenyl	72	210	56.01	3.45	12.46
6	f	4-methoxyphenyl	85	219	55.30	3.42	12.45
7	g	2-hydroxyphenyl	84	198	58.20	3.44	12.97
8	h	4-methylphenyl	76	207	57.70	3.24	12.72
9	i	3,4,5-triimethoxyphenyl	74	216	57.30	4.42	11.60
10	j	3-phenoxyphenyl.	71	215	59.60	4.14	11.72

IR Spectral Studies

No.	Code	-N-CO-N-	-$NCOCH_3$	-NH-	-C-R
1	a	1355	1256	3204	-
2	b	1336	1255	3206	2836
3	c	1374	1264	3202	2832
4	d	1355	1265	3213	3444
5	e	1333	1256	3196	675
6	f	1316	1267	3213	676
7	g	1355	1279	3217	1321
8	h	1352	1253	3222	616
9	i	1347	1276	3212	2824
10	j	1366	1244	3201	2836

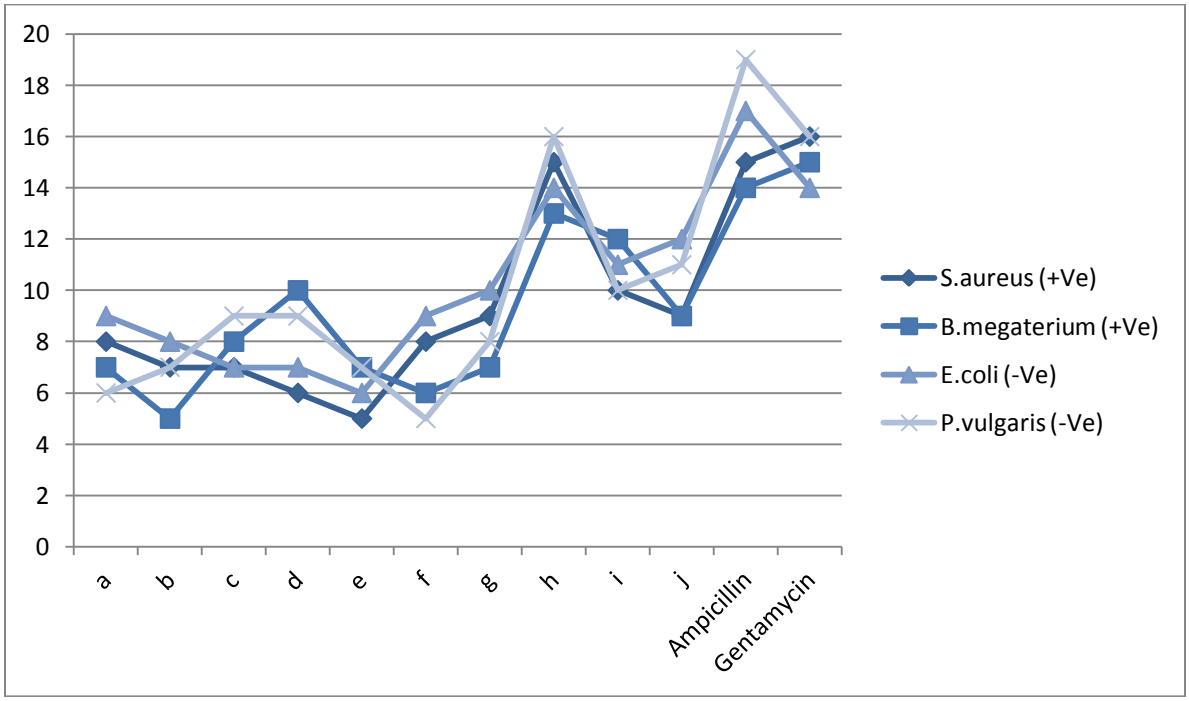
IR Spectra of sample code (f)



ANTIMICROBIAL ACTIVITY

The medicament activity of the compounds was screened by disc plate technique. The take a look at discs were containing fifty metric weight unit per disc of the take a look at compound. The activity was shown against gram positive bacterium area unit coccus aureus, Bacillus megaterium and gram negative bacteria Escherichia coli, Proteus vulgaris.[VIII-XI]

The antimicrobial activities of recently synthesised compounds were compared with proverbial antibiotics like Polycillin and Gentamycin; all the compounds show moderate to sensible activity



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Comparison of 1H-Pyrazol Derivative against Standard Drugs

Organisms	Compounds	Ampicillin	Gentamycin
S.aureus	h	-	✓
B. megaterium	h	✓	-
E.coli	i	-	✓
P. vulgaris	h	-	✓

Conclusion:
The screening results revealed that the Compound h & i shows significant results against gram positive and gram negative bacteria respect to standard drug Ampicillin and Gentamycin.

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