© 2016 IJSRSET | Volume 2 | Issue 6 | Print ISSN: 2395-1990 | Online ISSN : 2394-4099
Themed Section: Engineering and Technology

Synthesis of Credible Fluoro Nitro Containg Novel Benzopyrimidi

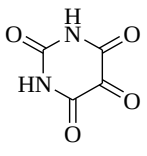
J. R. Shukla[1*], Vikas Chauhan[2]
[1]Department of Chemistry, Shri C.N.P.F Arts & D. N.Science College, Dabhoi, Gujarat, India
[2]Asstanr Manager, Apothecon Pharmaceutical, Dabhasa, Gujarat, India

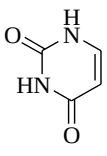
ABSTRACT

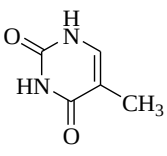
Synthesis of a series of N-(substituted phenyl)-2-methyl-4-(4-(4-(trifluoro methyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a] benzimidazole-3-carboxamide products ***(4a-j)*** was completed from 4-(4-(trifluoromethyl)-2-nitrophenoxy)benzaldehyde, N-(substitutedphenyl)-3-oxobutanamides and using 2-amino benzimidazole in DMF reflux for 24 hrs, the product obtained was isolated. So to the outstanding yield. The structures of the products were supported by FTIR, ^{1}H NMR and mass spectral data.
Keywords : N-(substitutedphenyl)-3-oxobutanamides, 4-(4-(trifluoromethyl)-2-nitrophenoxy)benzaldehyde, 2-amino benzimidazole and DMF only refluxed.

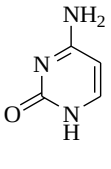
I. INTRODUCTION

Heterocyclic nucleus imparts an important role in medicinal chemistry and serves as a key template for the development of various therapeutic agents. In an ecological and financial perspective it is becoming evident that the conventional methods of performing arts chemical synthesis are indefensible and have to be changed. Multicomponent coupling reactions offer a solution since they are well-organized, cost efficient and less extravagant than conventional process. The products of temperature responsive reactions from kinetic path can be selectively isolated. Since multicomponent reactions often generate complete and complex molecular products in a single synthetic, it is more precise to describe this modern organic chemistry. Alloxan is known for its diabetogenic action in a number of animals [1]. Uracil, thymine and cytosine are the three important constituents of nucleic acids.


Alloxan


Uracil

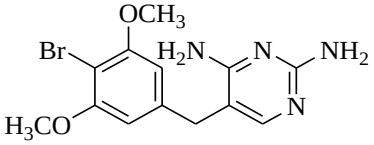

Thymine


Cytosine

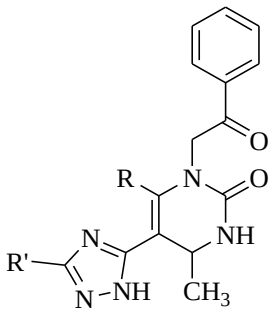
Medicinal Significance of Pyrimidine

There are a large number of pyrimidine-based antimetabolites. They are usually structurally related to the endogenous substrates that they antagonize. The structural modification may be on the pyrimidine ring or on the pendant sugar groups. One of the early metabolites prepared was 5-fluorouracil [2, 3] a pyrimidine derivative. 5- Thiouracil also exhibits some useful antineoplastic activities [4] the antineoplastic compounds [5] possessing the guanine nucleus like azathioprine [6], mercaptopurine [7], thioguanine [8], tegafur [9], etc.

Antimicrobial Activity: Microbes cause various types of disease like pneumonia, amoebiasis, typhoid, malaria, cough and cold infections and some severe diseases like tuberculosis, influenza, syphilis, and AIDS as well. Kompis I and Co-workers [10] synthesized Brodimoprim, and found it to be an effectiveantibacterial compound.

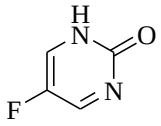

Brodimoprim

Polak A. and Co-workers [11] proved that Pyrimidine also shows antifungal properties. Flucytosine is a fluorinated pyrimidine used as nucleosidal anti fungal agent for the treatment of serious systemic infections caused by susceptible strains of candida and Cryptococcus. And Mishra A. and co-workers [12] synthesized various derivatives of pyrimidines and reportedtheir fungicidal activities against P .infestans and C. falcatum by the usual agar plate method.



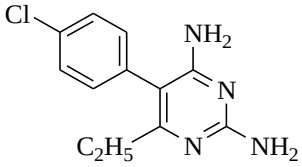
R= m-nitrobenzene, p-methoxybenzene

R'= phenyl, p-chlorobenzene..

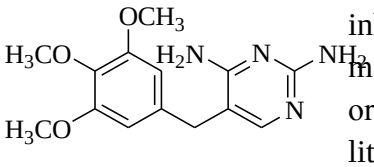


Flucytosine

Cheng CC and Co-Workers [13] showed that 2, 4-diaminopyrimidine drugs, pyrimethamine is a selective inhibitor of the DHFR of malarial plasmodia and trimethoprim, an antibacterialdrug is also a selective inhibitor and selectively inhibits bacterial DHFR.

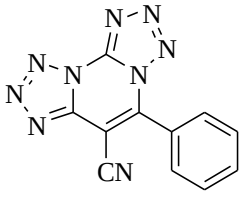


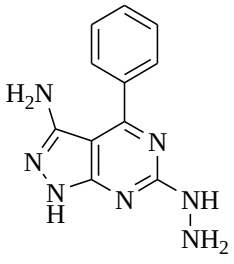
Pyrimethamine



Trimethoprim

Aly A.A [14], synthesized a series of 1- glycosyl thiopyrimidines, annulated pyrimidines derivatives, pyrazolo [3, 4-d] pyrimidines, ditetrazolo [1, 5- a, 1, 5'-c] pyrimidines thieno [2, 3-d] pyrimidines derivative. The antimicrobial activity was determined in vitro using cup plate and paper disc method.



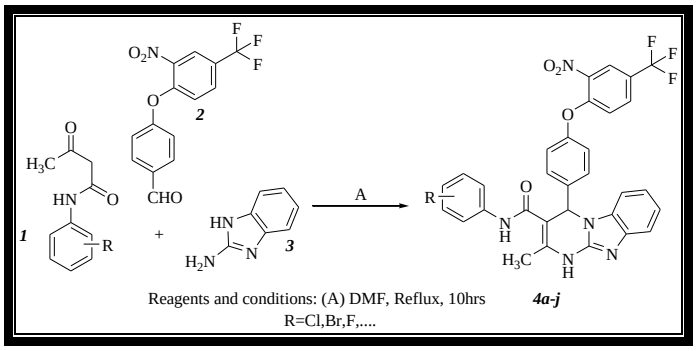


Fahmy HTY [15] and Co-workers: synthesized a series of novel fluorinated thiazolo[4,5-d] pyrimidine derivatives and sceened their anticancer activity against 60 human tumor cell lines. Compounds showed better anticancer activity against tumor cell lines. Jerzy Cleplik, et al [16] Synthesized of 1,2,3,4 tetra aryl 1,2,3,4 –tetra hydropyrimido [4,5-d] pyrimidines. The structures of obtained compounds were confirmed by crystallographic and spectroscopic analyses and their antibacterial activity was tested on 9 selected strains.

Benzimidazole Containing Pyrimidine Derivatives

There are c.a. 50 derivatives of 2-aminobenzimidazole registered in the world as drugs with anticancer, antiviral, antifungal, anthelmintic and antihistamine properties[17]. Based on a review of the chemical literature, derivatives of 2-aminobenzimidazole showed multipharmacological effects such as hypotensive effect [18], anti-inflammatory effects [19], analgesic [20] or antiaggregatory [21] activity. Some chemical compounds, which contain in their structure 2-aminobenzimidazole motif inhibitneurodegeneration and in the future they may be used in a treatment of Alzheimer's disease or Parkinson's disease [22]. Recently, a lot of literature has revealed that 2-amino-1H-benzimidazole derivatives could effectively inhibiting the growth of various microorganisms, which suggest that 2-aminobenzimidazole compounds should have large potential as a new type of antibacterial [23], antifungal [24] or antiviral [25] agents. Biological activity of 2-amino-1H-benzimidazole has been studied [26,27]. In our last review, we presented selected methods of synthesis for 2-amino-1H-benzimidazoles [28], drugs, containing in their structures 2-aminobenzimidazole compound [29], and new derivatives, which possess biological activity and their mechanism of action [30].

Reaction *S*cheme



II. METHODS AND MATERIAL

A mixture of the 2-amino benzimidazole (0.01 M), N-(substitutedphenyl)-3-oxobutanamide (0.02 M) and 4-(4-(trifluoromethyl)-2-nitrophenoxy)-2-hydroxybenzaldehyde (0.01 M) was refluxed in DMF (10 ml) for 24 hrs. After cooling, methanol (~25 ml) was added. The reaction mixture was allowed to stand overnight and then filtered to give the solid N-(substituted phenyl)-2-methyl-4-(4-(4-(trifluoro methyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a] benzimidazole-3-carboxamide products **(4a-j)**, which were recrystallized from ethanol.

N-(phenyl)-2-methyl-4-(4-(4-(trifluoro methyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4a)

Yield: 60%; mp 180ºC; MS: *m/z* 586; IR (cm^{-1}): 3471 (N-H stretching of secondary aminde), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2857 (C-H asymmetrical stretching of CH_3 group), 1657 (C=O stretching of amide), 1607 (N-H deformation of pyrimidine ring), 1537 (C-NO2 stretching), 1491 (C=C stretching of aromatic ring), 1396 (C-H asymmetrical deformation of CH_3 group), 1347 (C-H symmetrical deformation of CH_3 group), 1274 (C-N stretching), 1167 (C-H in plane deformation of aromatic ring), 1076 (C-F stretching), 829 (C-H out of plane bending of 1,4-disubstituion); ^{1}H NMR (DMSO-d_6) δ ppm: 1.22 (s, 3H, H), 5.3-5.33 (s, 1H, H), 7.07- 7.10 (dd', 2H, H), 7.23-7.24 (dd', 2H, H), 7.32-7.34 (dd', 2H, H), 7.37-7.38 (dd', 2H, H), 7.47-7.52 (m, 3H, H), 7.87-7.95 (dd', 2H, H), 8.42-8.45 (m, 3H, H), 8.87-8.88 (s, 1H, H), 10.02 (s, 1H, H); Anal. Calcd. for $C_{31}H_{22}F_3N_5O_4$: C, 64.59; H, 4.79; F, 9.73; N, 11.96; O, 10.93; Found: C, 64.65; H, 4.76; F, 9.70; N, 11.99; O, 10.90%.

N-(4-chlorophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4b)

Yield: 60%; mp 197ºC; MS: *m/z* 620; IR (cm^{-1}): 3254 (N-H stretching of secondary amine), 3105 (C-H stretching of aromatic ring), 2935 (C-H asymmetrical stretching of CH_3 group), 2838 (C-H asymmetrical stretching of CH_3 group), 1665 (C=O stretching of amide), 1595 (N-H deformation of pyrimidine ring), 1527 (C-NO2 stretching), 1477 & 1429 (C=C stretching of aromatic ring), 1342 (C-H asymmetrical deformation of CH_3 group), 1307 (C-H symmetrical deformation of CH_3 group), 1254 (C-N stretching), 1195 (C-H in plane deformation of aromatic ring), 1095 (C-F stretching), 835 (C-H out of plane bending of 1,4-disubstituion), 695 (C-Cl stretching); Anal. Calcd. for $C_{31}H_{21}ClF_3N_5O_4$: C, 60.06; H, 3.41; Cl, 5.72; F, 9.19; N, 11.30; O, 10.32; Found: C, 60.02; H, 3.45; Cl, 5.71; F, 9.20; N, 11.32; O, 10.30%.

N-(3-chlorophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4c)

Yield: 67%; mp 198ºC; MS: *m/z* 620; IR (cm^{-1}): 3200 (N-H stretching of secondary amine), 3045 (C-H stretching of aromatic ring), 2925 (C-H asymmetrical stretching of CH_3 group), 2862 (C-H asymmetrical stretching of CH_3 group), 1664 (C=O stretching of amide), 1595 (N-H deformation of pyrimidine ring), 1456 (C-NO2 stretching), 1405 (C=C stretching of aromatic ring), 1340 (C-H asymmetrical deformation of CH_3 group), 1311 (C-H symmetrical deformation of CH_3 group), 1250 (C-N stretching), 1211 (C-H in plane deformation of aromatic ring), 1020 (C-F stretching), 834 (C-H

out of plane bending of 1,4-disubstituion), 640 (C-Cl stretching); Anal. Calcd. for $C_{31}H_{21}ClF_3N_5O_4$: C, 60.06; H, 3.41; Cl, 5.72; F, 9.19; N, 11.30; O, 10.32; Found: C, 60.07; H, 3.40; Cl, 5.72; F, 9.23; N, 11.33; O, 10.33%.

N-(4-bromophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4d)

Yield: 73%; mp 189ºC; MS: *m/z* 664; IR (cm^{-1}): 3300 (N-H stretching of secondary aminde), 3088 (C-H stretching of aromatic ring), 3059 (C-H asymmetrical stretching of CH_3 group), 2926 (C-H asymmetrical stretching of CH_3 group), 1639 (C=O stretching of amide), 1568 (N-H deformation of pyrimidine ring), 1502 (C-NO2 stretching), 1454 (C=C stretching of aromatic ring), 1329 (C-H asymmetrical deformation of CH_3 group), 1302 (C-H symmetrical deformation of CH_3 group), 1219 (C-N stretching), 1109 (C-H in plane deformation of aromatic ring), 1045 (C-F stretching), 832 (C-H out of plane bending of 1,4-disubstituion), 655 (C-Br stretching); Anal. Calcd. for $C_{31}H_{21}NBrF_3N_5O_4$: C, 56.04; H, 3.19; Br, 12.03; F, 8.58; N, 10.54; O, 9.63; Found: C, 56.06; H, 3.20; Br, 12.06; F, 8.51; N, 10.50; O, 9.60%.

N-(3-bromophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4e)

Yield: 70%; mp 184ºC; MS: *m/z* 664; IR (cm^{-1}): 3377 (N-H stretching of secondary aminde), 3211 (C-H stretching of aromatic ring), 2959 (C-H asymmetrical stretching of CH_3 group), 2849 (C-H asymmetrical stretching of CH_3 group), 1647 (C=O stretching of amide), 1597 (N-H deformation of pyrimidine ring), 1545 (C-NO2 stretching), 1507 (C=C stretching of aromatic ring), 1433 (C-H asymmetrical deformation of CH_3 group), 1340 (C-H symmetrical deformation of CH_3 group), 1244 (C-N stretching), 1178 (C-H in plane deformation of aromatic ring), 1066 (C-F stretching), 870 (C-H out of plane bending of 1,4-disubstituion), 644 (C-Br stretching); Anal. Calcd. for $C_{31}H_{21}NBrF_3N_5O_4$: C, 56.04; H, 3.19; Br, 12.03; F, 8.58; N, 10.54; O, 9.63; Found: C, 56.00; H, 3.24; Br, 12.08; F, 8.50; N, 10.52; O, 9.59%.

N-(4-fluorophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydro pyrimido[1,2-a] benzimidazole-3-carboxamide (4f)

Yield: 60%; mp 173ºC; MS: *m/z* 604; IR (cm^{-1}): 3255 (N-H stretching of secondary aminde), 3050 (C-H stretching of aromatic ring), 2976 (C-H asymmetrical stretching of CH_3 group), 2952 (C-H asymmetrical stretching of CH_3 group), 1665 (C=O stretching of amide), 1595 (N-H deformation of pyrimidine ring), 1455 (C-NO2 stretching), 1404 (C=C stretching of aromatic ring), 1345 (C-H asymmetrical deformation of CH_3 group), 1311 (C-H symmetrical deformation of CH_3 group), 1274 (C-N stretching), 1122 (C-H in plane deformation of aromatic ring), 1030 (C-F stretching), 790 (C-H out of plane bending of 1,4-disubstituion); Anal. Calcd. for $C_{31}H_{21}F_4N_5O_4$: C, 61.69; H, 4.51; F, 12.59; N, 11.60; O, 10.60; Found: C, 61.68; H, 4.50; F, 12.54; N, 11.65; O, 10.62%.

N-(3-fluorophenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a]benzimidazole-3-carboxamide (4g)

Yield: 73%; mp 171ºC; MS: *m/z* 604; IR (cm^{-1}): 3200 (N-H stretching of secondary aminde), 3034 (C-H stretching of aromatic ring), 2989 (C-H asymmetrical stretching of CH_3 group), 2889 (C-H asymmetrical stretching of CH_3 group), 1699 (C=O stretching of amide), 1608 (N-H deformation of pyrimidine ring), 1569 (C-NO2 stretching), 1458 (C=C stretching of aromatic ring), 1309 (C-H asymmetrical deformation of CH_3 group), 1278 (C-H symmetrical deformation of CH_3 group), 1195 (C-N stretching), 1109 (C-H in plane deformation of aromatic ring), 1045 (C-F stretching), 833 (C-H out of plane bending of 1,4-disubstituion); Anal.

Calcd. for $C_{31}H_{21}F_4N_5O_4$: C, 61.69; H, 4.51; F, 12.59; N, 11.60; O, 10.60; Found: C, 61.70; H, 4.52; F, 12.50; N, 11.63; O, 10.64%.

N-(4-methylphenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a]benzimidazole-3-carboxamide (4h)

Yield: 70%; mp 184ºC; MS: *m/z* 600; IR (cm^{-1}): 3200 (N-H stretching of secondary aminde), 3078 (C-H stretching of aromatic ring), 2938 (C-H asymmetrical stretching of CH_3 group), 2808 (C-H asymmetrical stretching of CH_3 group), 1718 (C=O stretching of amide), 1612 (N-H deformation of pyrimidine ring), 1590 (C-NO2 stretching), 1450 (C=C stretching of aromatic ring), 1398 (C-H asymmetrical deformation of CH_3 group), 1319 (C-H symmetrical deformation of CH_3 group), 1218 (C-N stretching), 1136 (C-H in plane deformation of aromatic ring), 998 (C-F stretching), 856 (C-H out of plane bending of 1,4-disubstituion); Anal. Calcd. for $C_{32}H_{24}F_3N_5O_4$: C, 64.10; H, 4.03; F, 9.51; N, 11.68; O, 10.67; Found: C, 64.08; H, 4.05; F, 9.57; N, 11.69; O, 10.60 %;

N-(4-methoxyphenyl)-2-methyl-4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a]benzimidazole-3-carboxamide (4i)

Yield: 53%; mp 180ºC; MS: *m/z* 616; IR (cm^{-1}): 3181 (N-H stretching of secondary aminde), 3081 (C-H stretching of aromatic ring), 2956 (C-H asymmetrical stretching of CH_3 group), 2850 (C-H asymmetrical stretching of CH_3 group), 1714 (C=O stretching of amide), 1611 (N-H deformation of pyrimidine ring), 1592 (C-NO2 stretching), 1450 (C=C stretching of aromatic ring), 1377 (C-H asymmetrical deformation of CH_3 group), 1321 (C-H symmetrical deformation of CH_3 group), 1261 (C-N stretching), 1132 (C-H in plane deformation of aromatic ring), 991 (C-F stretching), 748 (C-H out of plane bending of 1,4-disubstituion); Anal. Calcd. for $C_{32}H_{24}F_3N_5O_5$: C, 62.44; H, 4.93; F, 9.26; N, 11.38; O, 14.00; Found: C, 62.42; H, 4.95; F, 9.25; N, 11.33; O, 14.05%.

N-(4-nitrophenyl)-2-methyl-4-(4-(4-(trifluoro methyl)-2-nitrophenoxy) phenyl)-1,4-dihydropyrimido[1,2-a]benzimidazole-3-carboxamide (4j)

Yield: 57%; mp 179ºC; MS: *m/z* 631; IR (cm^{-1}): 3360 (N-H stretching of secondary aminde), 3082 (C-H stretching of aromatic ring), 2956 (C-H asymmetrical stretching of CH_3 group), 2848 (C-H asymmetrical stretching of CH_3 group), 1670 (C=O stretching of amide), 1600 (N-H deformation of pyrimidine ring), 1562 (C-NO2 stretching), 1460 (C=C stretching of aromatic ring), 1390 (C-H asymmetrical deformation of CH_3 group), 1327 (C-H symmetrical deformation of CH_3 group), 1263 (C-N stretching), 1140 (C-H in plane deformation of aromatic ring), 1062 (C-F stretching), 837 (C-H out of plane bending of 1,4-disubstituion); Anal. Calcd. for $C_{31}H_{21}F_3N_6O_6$: C, 59.05; H, 4.36; F, 9.04; N, 14.33; O, 15.22; Found: C, 59.06; H, 4.37; F, 9.07; N, 14.30; O, 15.20%.

III. RESULTS AND DISCUSSION

Biological evaluation

Antimicrobial evaluation

Total of the Prepared compounds were experienced for their antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method[31-33]with two Gram-positive bacteria ***Staphylococcus aureus*** MTCC-96, ***Streptococcus pyogenes*** MTCC 443, two Gram-negative bacteria ***Escherichia coli*** MTCC 442, ***Pseudomonas aeruginosa*** MTCC 441 and three fungal strains ***Candida albicans*** MTCC 227, ***Aspergillus Niger*** MTCC 282, ***Aspergillus clavatus*** MTCC 1323 taking **gentamycin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and greseofulvin** as regular drugs.

The minimal inhibitory concentration (MIC) values for all the newly synthesized compounds, definited as the lowly concentration of the compound preventing the observable growth, were determined by using micro dilution broth method according to NCCLS standards [61].

Minimal Inhibition Concentration [MIC]:-

The main advantage of the 'Broth Dilution Method' for MIC determination lies in the fact that it can readily be converted to determine the MIC as well.

- Serial dilutions were prepared in primary and secondary screening.
- The control tube containing no antibiotic is immediately subcultured (before inoculation) by spreading a loopful evenly over a quarter of plate of medium suitable for the growth of the test organism and put for incubation at 37 ^{0}C overnight.
- The MIC of the control organism is read to check the accuracy of the drug concentrations.
- The lowest concentration inhibiting growth of the organism is recorded as the MIC.
- The amount of growth from the control tube before incubation (which represents the original inoculums) is compared.

Table-1:- *in vitro Antimicrobial Screening Results for* (4a-j)

Code	**Minimal inhibition concentration (μg mL^{-1})**						
	Gram-positive		**Gram-negative**		**Fungal species**		
	S.a.	***S. p.***	***E.c.***	***P.a.***	***C. a.***	***A. n.***	***A.c.***
4a	>1000	320	450	450	450	320	350
4b	450	350	100	320	350	450	350
4c	100	320	>1000	350	350	350	350
4d	350	>1000	450	320	450	450	450
4e	450	450	>1000	450	450	450	320
4f	450	450	450	450	450	100	450
4g	320	>1000	320	450	350	350	450
4h	320	350	320	450	350	450	450
4i	450	>1000	450	100	320	450	350
4j	300	450	450	350	>1000	100	320
Gentamycin	0.25	0.5	0.05	1	-	-	-
Ampicillin	245	100	100	100	-	-	-
Chloramphenicol	50	50	50	50	-	-	-
Iprofloxacin	50	50	25	25	-	-	-
Norfloxacin	10	10	10	10	-	-	-
Nystatin	-	-	-	-	100	100	100
Griseofulvin	-	-	-	-	450	100	100

IV. CONCLUSION

In construct, we acquire in make of imaginative pyrimidine derivatives using devoid of any plight and appropriate process. By method produces these products in high-quality yield and trouble-free work on. Product is isolated by effortless filtration. The isolated products are much uncontaminated and do not require any another purification.

V. REFERENCES

[1]. Eussell, J. A. Annu. Rev. Biochem. 1945, 14, 309.
[2]. Cox, R. A. Quart. Rev. 1968, 22, 934.
[3]. Callery, P.; Gannett, P. Cancer and cancer chemotherapy. In Foye's Principles of Medicinal Chemistry (eds Williams, D. A., Lemke, T. L.), Lippincott Williams and Wilkins, Philadelphia, 2002, 934.
[4]. Al Safarjalani, O. N.; Zhou, X. J.; Ras, R. H.; Shi, J.; Schinazi, R. F.; Naguib, F. N.; El Kouni, M. H. Cancer Chemother. Pharmacol. 2005, 55, 541.

[5]. Remers, W. A. Antineoplastic agents. In Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry (eds Delgado, J. N.; Remers, W. A.), Lippincott Williams and Wilkins, Philadelphia, 1998, 366.
[6]. Elion, G. B. Fed. Proc. 1967, 26, 898.
[7]. Burchenal, J. H. et al. Blood, 1953, 8, 965.
[8]. Clarkson, B. D. Cancer 1970, 5, 227.
[9]. Giller, S. A.; Zhuk, R. A.; Lidak, M. I. U. Dokl. Akad. Nauk. SSR 1967, 176, 332.
[10]. Kompis I and Wick A; Helv. Chim. Acta, 1977; 60: 3025.
[11]. Polak A. and Scholer HJ; Chemotherapy, 1975; 21: 113.
[12]. Mishra A and Singh DV; Indian J. Hetero. Chem, 2004; 14: 43-46.
[13]. Cheng CC and Roth B; In Progress in Medicinal Chem. (eds Ellis GP and West GB),Butterworths London; 1982; 19: 267.
[14]. Aly A.A., Chinese Journal of Chem, 2005; 23: 211-217.
[15]. Fahmy HTY, Rostom SAF, Saudi MN, Zjawiony JK, Robins DJ. Arch Pharm Pharm Med Chem, 2003; 3: 1-10.
[16]. Jerzy Cleplik, Marcin Stolarczyk, Januzy Pluta, Olaf Gubrynowicz,Iwona Bryndal, Tadeusz Lis & Marcin Mikulewicz.,Acta Poloniae Pharmaceutica-Drug Research.,2011, 68(1), 57.
[17]. The Merck Index, 14th edition (Whitehouse Station, USA, 2006).
[18]. V.A. Anisimova, M.M. Osipova, A.A. Spasov, A.F. Turchaeva, G.P. Dudchenko, N.P. Larionov, S.G. Kovalcv, Pharm. Chem. J. 36, 468 (2002) .
[19]. A. Settimo, G. Primofiore, F. Settimo, A.M. Marini, Il Farmaco 47, 1293 (1992)
[20]. J.P. Powers, S. Li, J.C. Jaen, J. Liu, N.P.C. Walker, Z. Wang, H. Wesche, Bioorg. Med. Chem. Lett. 16, 2842 (2006)
[21]. P.F. Asobo, H. Wahe, J.T.Mbafor, A.E. Nkengfack, Z.T. Fomum, E.F. Sophue, D. Döpp, J. Chem. Soc. Perkin Trans. 1, 457 (2001)
[22]. J. Madden, J.R. Dod, R. Godemann, J. Kraemer, M. Smith, M. Biniszkiewicz, D.J. Hallett, J. Barker, J.D. Dyekjaer, T. Hesterkamp, Bioorg. Med. Chem. Lett. 20, 5329 (2010)
[23]. P.P. Seth, E.A. Jefferson, L.M. Risen, S.A. Osgood, Bioorg.Med. Chem. 13, 1669 (2003)
[24]. S.O. Podunavac-Kuzmanović, D.D. Cvetkovic, CI&CEQ 17, 9 (2011)
[25]. T.A. Farghaly, N.A.A. Hafez, E.A. Ragab, H.M. Awad, M.M. Abdalla, Eur. J. Med. Chem. 45, 492 (2010)
[26]. (a) W.P. Nawrocka, Boll. Chim. Farm. 135, 18 (1996); (b) W.P. Nawrocka, A. Nowicka, H. Liszkiewicz, Wiad. Chem. 66, 811 (2012) (in Polish)
[27]. W.P. Nawrocka, A. Nowicka, H. Liszkiewicz, Wiad. Chem. 66, 839 (2012) (in Polish)
[28]. W.P. Nawrocka, A. Nowicka, Wiad. Chem. 67, 715 (2013) (in Polish)
[29]. A. Nowicka, W.P. Nawrocka, Wiad. Chem. 67, 695 (2013) (in Polish)
[30]. A. Nowicka, W.P. Nawrocka, Wiad. Chem. 67, 203 (2013) (in Polish)
[31]. National Committee for Clinical and Laboratory Standards, Method forDilution Antimicrobial Susceptibility Tests for Bacteria that GrowAerobically Approved Standard, fourth ed. NCCLS, Villanova, Italy, 1997,Document M 100-S7. S100-S157.
[32]. Isenberg, D. H. Essential Procedure for Clinical Microbiology, American Society for Microbiology, Washington, 1998.
[33]. Zgoda, J. R.; Porter, J. R. Pharm. Biol. 2001, 39, 221.