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Research Article

A REVIEW ON PYRIMIDINE CONTAINING HETEROCYCLIC COMPOUNDS

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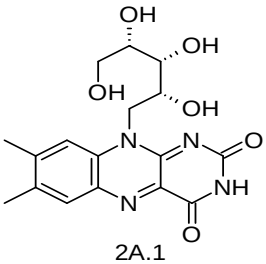
ABSTRACT

Many pyrimidine derivatives have been developed as chemotherapeutic agents and are widely used. Microbes are causative agents for various types of diseases like pneumonia, amoebiasis, typhoid, malaria, common cough and cold, various infections, and some severe diseases like tuberculosis, influenza, syphilis, and AIDS as well. In these reviews, we brought some characteristic and interesting features of the pyrimidine-containing heterocyclic moieties.

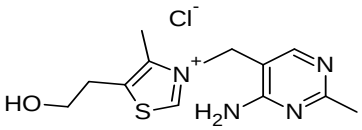
Keywords: *Pyrimidines, pneumonia, various infections, AIDS.*

1. INTRODUCTION:

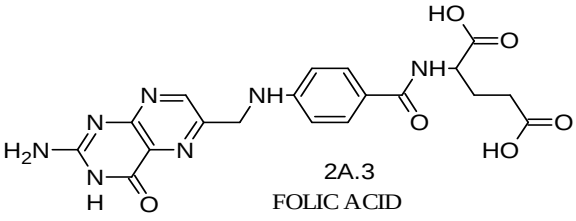
The practice of medicinal chemistry is devoted to the discovery and development of new agents for treating disease. The process of establishing a new drug is exceeding complex and involves the talent of people from a variety of disciplines[1]. An important aspect of medicinal chemistry has been to establish a relationship between chemical structure and pharmacological activity[2]. Pyrimidine is a six-membered cyclic compound containing 4 carbon and 2 nitrogen atoms and is pharmacologically inactive but its synthetic derivatives possess an important role in modern medicine. In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications. The presence of a pyrimidine base in thymine, cytosine, and uracil, which are the essential building blocks of nucleic acids, DNA, and RNA, is one of the possible reasons for their activities[3]. Vitamins are essential for the body. Pyrimidine ring is found in vitamins like riboflavin, thiamine, and folic acid[4].



2A.1
RIBOFLAVIN



2A.2
THIAMINE



2A.3
FOLIC ACID

Pyrimidine nucleus is also present in barbituric acid and its several derivatives e.g. Veronal which are used as hypnotics [5].

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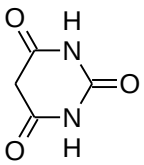
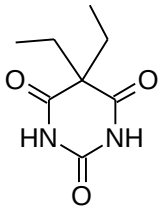
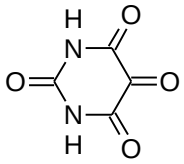


2A.4
BARBITURIC ACID



2A.5
VERONAL

In addition to this, pyrimidine nucleus is also found in alloxan, which is known for its diabetogenic action in a number of animals6.

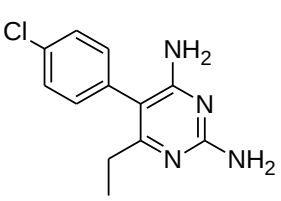


2A.6
ALLOXAN

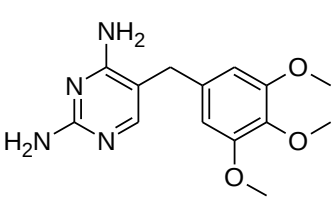
The pyrazolopyrimidine derivatives are an important class of heterocyclic compounds with pharmacological and biological activities, such as the antibacterial7 antiviral8 cytotoxic9 antidepressant10 neuroleptic11 tuberculostatic12 antihypertensive13 analgesic14 and antimicrobial activity.15 The pyrazolo[1,5-a]pyrimidines as bicyclic heterocycles have an important synthetic value in the preparation of drugs with anticancer activities.16-21 The most common methods for synthesis of pyrazolo[1,5-a]pyrimidine derivatives are cyclocondensations of 5-aminopyrazoles with bifunctional reagents.22 The synthesis of 2-anilinopyrazolo[1,5-a]pyrimidine derivatives as c-Src kinase inhibitors has been reported.23 In continuation of our studies on the synthesis of heterocycles,24-31 herein we report a microwave irradiation method for the synthesis of new pyrazolo[1,5-a]pyrimidine derivatives with possible pharmaceutical applications.

BRIEF REVIEW:

Hitchings32 in 1948, made an important observation that a large number of 2, 4 di amino pyrimidines and some 2-amino-4-hydroxy pyrimidines are antagonists of folic acid. These pyrimidines were than eventually proved as inhibitors of the enzyme dihydrofolate reductase (DHFR) by futterman33 & group in 1957. In 1982 cheng34 & group gave the information that amongst the 2, 4-diaminopyrimidine drugs, pyrimethamine is a selective inhibitor of the DHFR of malarial plasmodia. Trimethoprim, an antibacterial drug is also a selective inhibitor and selectively inhibits bacterial DHFR.

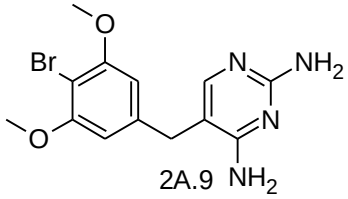


2A.7
PYRIMETHAMINE



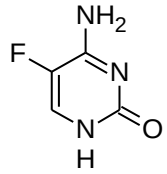
2A.8
TRIMETHOPRIM

Kompis35 & group in 1977 proved Brodimoprim, is an effective antibacterial compound.



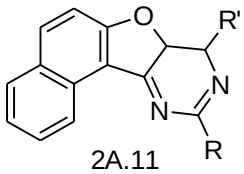
2A.9
BRODIMOPRIM

Polak36 & group in 1975 gave information that Pyrimidine also shows antifungal properties. Flucytosine is a fluorinated pyrimidine used as nucleosidal antifungal agent for the treatment of serious systemic infections caused by susceptible strains of Candida and Cryptococcus.



2A.10
FLUCYTOSINE

Padamshari & group 37 in 2002 synthesized Naptho [2, 1- b] furo [3, 2-a] pyrimidine which is useful in the preparation of pharmacologically active compound like anti-inflammatory, anti- antihelmintic and antimicrobial agents.

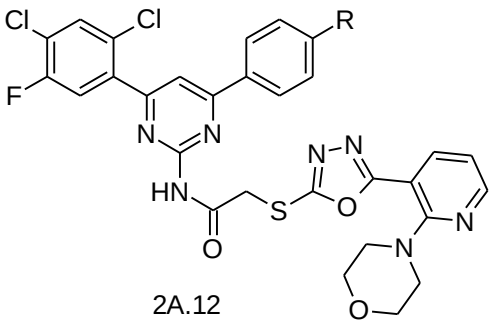


2A.11

R = CH_3, C_6H_5

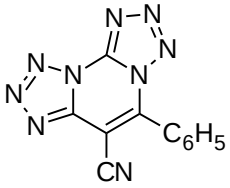
R"= OCH_3, OC_2H_5, NHC_2H_5, NHC_6H_5

Naik & group38 in 2007 synthesized 2-[{2 (Morpholino)-3-pyridinyl- 5- thio} - 2 oxoethyl oxadiazolyl]- amino- 4- (2, 4 dichloro- 5- fluorophenyl)- 6- (aryl) pyrimidines, which exhibit maximum zone of inhibition against E.coli, S. aureus, S.typhii and B.subtilis.

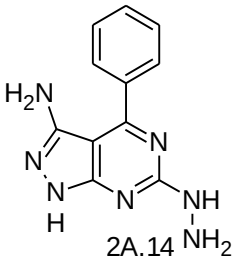


2A.12

R= 4-CH3-C6H4; 4-Cl-C6H4; 2, 4-(Cl)2-C6H3; 4-F-C6H4; 3, 4, 5-(OCH3)3-C6H2, Aly & group39 in 2005 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.

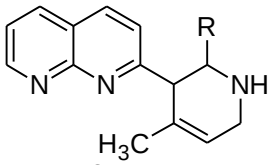


2A.13



2A.14

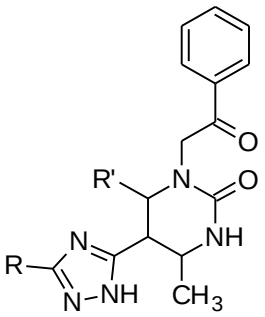
Mogilaiah & group 40 in 2003 reported 1, 8 Napthopyridine derivatives which were tested for their antibacterial activity in vitro against E. coli and B. subtilis using filter paper disc technique.



2A.15

Where R= C6H5, p-CH3C6H5, CH3OC6H4, o-ClC6H4, p-ClC6H4, p-OHC6H4

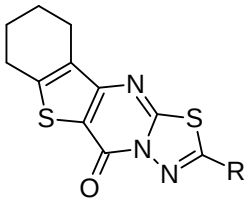
Mishra & group41 in 2004 synthesized various derivatives of pyrimidines. The fungicidal activities of the compound were evaluated against P. infestans and C. falcatum by the usual agar plate method.



2A.16

R= C6H5, p-ClC6H4, m-NO2C6H4, p-OCH3C6H4; R'= m-NO2C6H4, p- OCH3C6H4

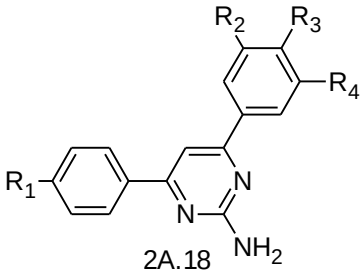
Alagarsamy & group42 in 2004 synthesized some 2 substituted (1, 3, 4) thiadiazole(2, 3-b) tetrahydro-benzothieno [3, 2-e] pyrimidines and then screened them for anticancer, antibacterial and antifungal activities.



2A.17

R= H, CH3, NHCH3, (CH2)2CH3

Rajesh Vyas & group43 in 2003 synthesized some 2 amino- 4, 6 diaryl substituted pyrimidines and then screened them for antibacterial and herbicidal activity.



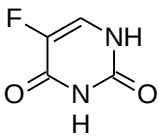
2A.18

R1= H, Cl, Br, OCH3; R2= OCH3, H; R3= OCH3, N (CH3)2; R4= OCH3, H

In other words it can be stated that pyrimidine moiety serves as a royal warrior against almost all types of microbes.

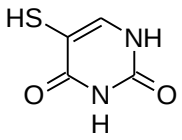
The pyrimidine moiety with some substitution shows promising antitumor activity as there are large numbers of pyrimidine based antimetabolites. The structural modification may be on the pyrimidine ring or on the pendant sugar & groups. Early metabolite prepared was 5-fluorouracil44, a pyrimidines followed by 5- Thiouracil which also exhibits some useful antineoplastic activities 45.

5-FLUOROURACIL



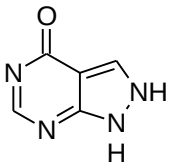
2A.19

5-THIOURACIL



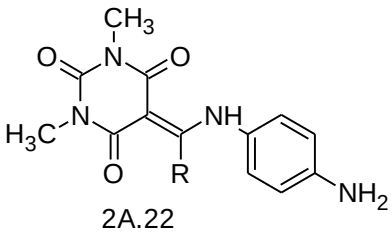
2A.20

ALLOPURINOL



2A.21

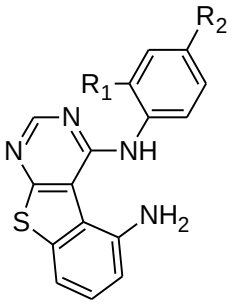
Palwinder Singh & group46 in 2008 reacted 5 benzoyl/ 5-carbaldehyde-/ 5- (3- phenyl acryloyl o- 6- hydroxy- 1H-pyrimidine- 2, 4 diones with amines provided the corresponding enamines. The investigation for anticancer activity of molecule at 59 human tumor cell lines was done representing leukemia, melanoma and cancer of lung, colon, brain, ovary, breast as well as kidney.



2A.22

R = H, CH=CH-Ph, Ph

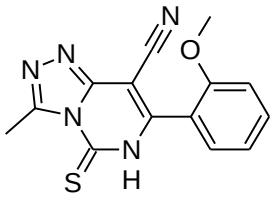
Stephane pedeboscq & group 47 in 2010 synthesized 4-(2-Methylanilino) benzo[b] thieno [2, 3-d] pyrimidine (1) and 4-(2-Methoxyanilino) benzo [b] thieno[2, 3-d]pyrimidine (2) which showed a similar cytotoxicity to the standard anti-EGFR geftinib suggesting a blockade of the EGFR pathway by binding to the tyrosine kinase receptor.



2A.23 a-b

R1= CH3 R2= H for (2A.23a)
R1= OCH3 R2= H for (2A.23b)

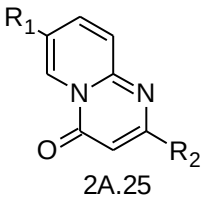
Fathalla & group48 in 2009 synthesized a series of some new pyrimidine derivatives like 7-(2-methoxyphenyl)-3-methyl-5-thioxo-5, 6-dihydro[1, 2, 4]-triazolo[4, 3-c]pyrimidine-8-carbo-nitrile via reaction of ethyl cyanoacetate with thiourea and the appropriate aldehydes namely 2-methyl-benzaldehyde and 2-methoxy-benzaldehyde followed via reaction with different reagents. All structures were than screened for bacterial activity and anticancer activity.



2A.24

Organic compounds and their complex with various ligands have found many applications in biomedicine.

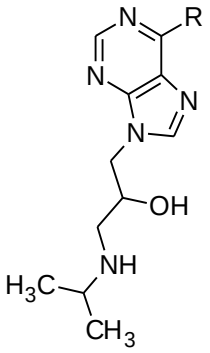
Al Allaf & group49 in 1996 describe the preparation of R2SnCl2 complex of some 4 H-pyrido [1, 2-a] pyrimidin-4-one derivatives as donating ligand having multiple donor sites and examine the cytotoxic activity of some of these complex against fine tumor cell lines.



2A.25

R1 = H, 7-CH3, 8-CH3; R2 = 2-CH2Br, 3-CH3COO

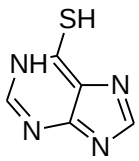
Silvana Raic-Malic & group50 in 1999 synthesized the novel purine and pyrimidine nucleoside analogues possessing a 2, 3-epoxypropyl, 2, 3-epoxypropyl ether, or 3-amino-2-hydroxypropyl moiety bonded at either N-9 of the C-6 substituted purine ring or N-1 and N-3 of the pyrimidine ring and were evaluated for their antitumour and antiviral activities.



2A.26

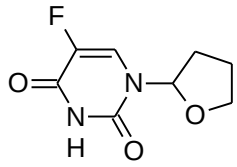
R= NH2, NHCH(CH3)2,

Guanine nucleus containing antineoplastic compounds like mercaptopurine51, tegafur52 etc. were discovered after formulation of antimetabolite theory 53.



2A.27

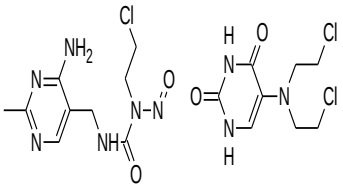
MERCAPTOPURINE



2A.28

TEGAFUR

Recently, new compounds have been developed like nimustine 54, uramustine 55, raltitrexed 56 etc.

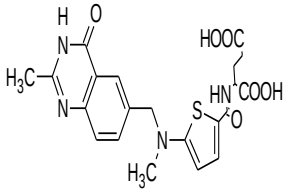


2A.29

NIMUSTINE

2A.30

URAMUSTINE

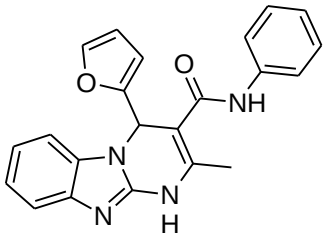


2A.31

RALTITREXED

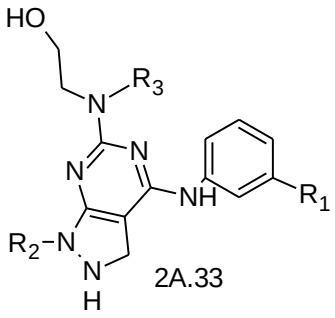
Fu RG57 & co-workers designed, synthesized four series of dihydropyrazolo[3,4-b]pyridines and benzo[4,5]imidazo[1,2-a]pyrimidines as dual KSP and Aurora-A kinase inhibitors. A

total of 19 target compounds were evaluated by two related enzyme inhibition assays and a cytotoxicity assay in vitro. The results showed that some target compounds could inhibit both enzymes and several of them showed significant inhibition activity against HCT116 cell line. Despite showing moderate KSP and Aurora-A kinase inhibition, the lead compound displayed significant cytotoxic activity in the micro molar range, especially against the HCT116 cell line and HepG2 cell line. The results may be useful for developing a new class of inhibitors having a dual function, KSP inhibition and Aurora-A kinase inhibition, for the treatment of cancer.



2A.32

Kim D. C58 & group in 2003 synthesized a series of 1,4,6-trisubstituted pyrazolo[3,4-d]pyrimidines capable of selectively inhibiting CDK2 activity by derivatization at C-4, C-6 and N-1 with various amines and lower alkyl & group s. In this series, 4-anilino compounds exhibited better CDK2 inhibitory activity and antitumor activity compared to 4-benzyl compounds. The compounds having a 3-fluoroaniline & group at C-4 showed comparable or superior CDK2 inhibitory activity to those of olomoucine and roscovitine as reference compounds. In general, the unsubstituted compounds at N-1 possessed higher potency than the substituted compounds for the CDK2 inhibitory activity. As for EGFR inhibitory activity, most compounds did not have a significant activity. The compounds exhibited potent cell growth inhibitory activity against human cancer cell lines, but their CDK2 inhibitory activities were slightly poorer than olomoucine.



2A.33

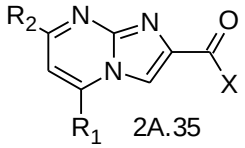
$R_1 = F \quad R_2 = H \quad R_3 = H$

Schenone & group59 in 2004 carried out synthesis of a new class of 1-aryl-4-amino-1H-pyrazolo[3,4-d]pyrimidine derivatives and evaluated for anticancer activity. It shows that the new compounds are potent inhibitors of cell growth.

2A.34 a-c

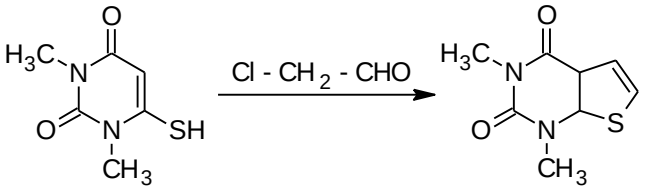
	R	R'
2A.34a	NH Cyclopropyl	$CH_2CHClPh$
2A.34b	NHC_3H_7	$CH_2CHClPh$
2A.34c	1-Pyrrolidinyl	$CH_2CHClPh$

Abignente & group 60 in 1994 synthesized compounds were tested for invivo anti-inflammatory and analgesic activity as well as their ulcerogenic activity. Three of the synthesized compounds showed good anti-inflammatory activity in rat paw edema method, while the same compounds show significant analgesic activity in acetic acid writhing method. The newly synthesized compounds were found to be lacking in inhibitory activity on cyclooxygenase invitro.



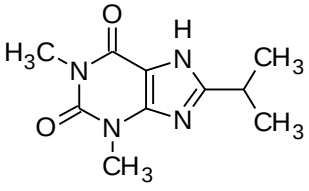
2A.35

Kosaku & group61 in 1990 reported the synthesis of 6-substituted thieno [2,3-d] pyrimidine-2,4(1 H, 3H)-diones [1] by reaction of chloro acetaldehyde followed by cyclization to give desired molecule.



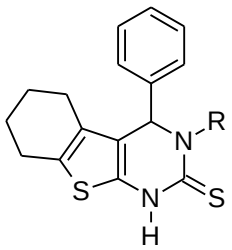
2A.36 2A.37

Bruno62 and co-workers in 1994 synthesized 8-N-aryl amino theophyllines (2N-aryl amino-4, 6-dimethylimidazo [4,5d] pyrimidine- (4H, 6H)-5, 7-diones) [2] staring from l,3-dimethyl-6-amino uracil.



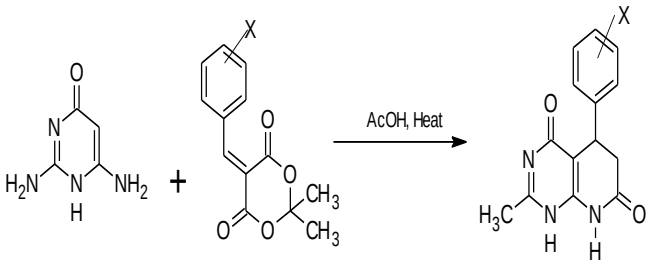
2A.38

Salvador Vega63 & group in 1990 reported 3-substituted-4-phenyl-2-thixo-l, 2,3,4,5,6,7,8-octahydrobenzo[4,5] thieno[2,3 d] pyrimidine.



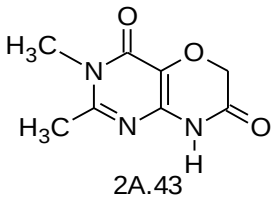
2A.39

Nazario64 & group in 1997 reported the synthesis of 2-amino-5-aryl-l, 4,5,6,7,8-hexahydro-4,7-dioxopyri[2,3 d] pyrimidines containing dihydropyridine ring system.



2A.40 2A.41 2A.42

Benjamin65 and co-workers in 1990 have synthesized and evaluated the cardiotonic activity of pyrimidol [5,4-b] [l,4]oxazinones.



2A.43

Conclusion: In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications. Many pyrimidine derivatives have been developed as chemotherapeutic agents and are widely used. Microbes are causative agents for various types of disease like pneumonia, amoebiasis, typhoid, malaria, common cough and cold, various infections and some severe diseases like tuberculosis, influenza, syphilis, and AIDS as well. Various approaches were made to check the role of pyrimidine moiety as antimicrobial agent from the discovery of molecule to the present scenario.

Reference:

1. Delgado J. N, Remers W. A, Wilson and Giswold's (1998).Textbook of Organic Chemistry Medicinal and Pharmaceutical Chemistry. 10th ed. Philadelphia: Lippincott Raven.
2. Miller D (1995). Remington- The Science and Practice of Pharmacy. 19th edition, 425.
3. Amir M, Javed S. A and Kumar H (2007). Indian J. Pharm. Sciences. 69, 3, 337-343.
4. Cox R. A (1968) Quart. Rev. Chem.Soc. 22, 499-526.
5. Jain M. K (2008). Sharnevas SC, Organic Chem.3, 997-999.
6. Eussell J. A., Annu(1945).Rev. Biochem. 14, 309-332.
7. Bayomi S. M., Amin K. M., Al-obaid A. M., Hares N. G(1993).Egypt J. Pharm. Sci. 34, 117-130.
8. Holla B. S, Kalluraya B, Sridhar K. R., Drake E, Thomas, L. M, Bhandary K. K, Levine M. J(1994). Eur. J. Med. Chem. 29, 4, 301-308.
9. Panisheva E. R., Kaplina N. V, Nikolaeva I. S, Phuskina T. V, Pershin Khim-Farm Z. H (1981). Chem. Abst. 15, 9, 40.
10. Abdou I. M, Saleh A. M, Zohdi H. F(2004). Molecule. 9, 3, 109-116.
11. Filler R (1974).Chem Technol. 4, 752-757.
12. Moustafa M. G, ZeinabH. I, Soad A. A, Hetero. Chem.1, 57-62.
13. EI-Feky A, Abd-Ei-Samii Z. K (1996). Pharmazie. 51, 540-543.
14. Vijaya Raj K. K, Narayan B. V, Ashalatha N, Suchita K(2006). J. Pharmacol. Toxicol.1, 6, 559-565.
15. Amin M. A, Iamil M. M, Addel G. A, Bauomy A. H, Ahmad M, Alexandria (2003). J. Pharm. Sci. 17, 1-11.
16. Lane M. E, Yu B, Rice A, Lipson K. E, Liang C, Sun L, Tang C, McMahon G, Pestell R. G, Wadler S(2001). Cancer Res. 61, 16, 6170-6177.
17. Fraley M. E, Hoffman W. F, Rubino R. S, Hungate R. W, Tebben A. J, Rutledge R. Z, McFall R. C, Huckle W. R, Kendall R. L, Coll K. E, Thomas K. A (2002). Bioorg. Med. Chem. Lett. 12, 19, 2767-2770.
18. Fraley M. E, Rubino R. S, Hoffman W. F, Hambaugh S. R, Arrington K. L, Hungate R. W, Bilodeau M. T, Tebben A. J, Rutledge R. Z, Kendall R. L, McFall R. C, Huckle W. R, Coll K. E, Thomas K. A (2002). Bioorg. Med. Chem. Lett. 12, 24, 3537-3541.
19. Wu Z, Fraley ME, Bilodeau M. T, Kaufman M. L., Tasber E. S, Balitza A. E, Hartman G. D, Coll K. E, Rickert K, Shipman J, Shi B, Sepp-Lorenzino L, Thomas K. A (2004). Bioorg. Med. Chem. Lett. 14, 909.
20. Arora A, Scholar E. M (2005). J. Pharmacol. Exp. Ther. 315, 971.
21. Meijer L, Raymond A. E. Acc (2003). Chem. Res. 36, 417-425.
22. Senga K, Novinson T, Wilson H. R (1981). J. Med. Chem. 24, 610.
23. Mukaiyama H, Nishimura T, Shiohara H, Kobayashi S, Komatsu Y, Kikuchi S, Tsuji E, Kamada N, Ohnota H, Kusama H (2007). Chem. Pharm. Bull. 55, 881.
24. Molla Ebrahimlo A. R, Khalafy J, Prager R H, Aust (2009). J. Chem. 62, 126.
25. Molla Ebrahimlo A. R, Khalafy J, Poursattar Marjani A, Prager R H, Arkivoc (2009). 12, 17-30.
26. A. Poursattar Marjani, Khalafy, (2011). J. Chem. Heterocycl. Comp. 47, 96.
27. Poursattar Marjani, Khalafy J, Molla Ebrahimlo A. R(2011). Synth. Commun. 41, 2475-2482.
28. Poursattar Marjani, Khalafy, J, Molla Ebrahimlo A. R, Prager R. H. Bull(2011) Korean. Chem. Soc. 32, 7, 2183.
29. Poursattar Marjani, Khalafy J, Prager, R. H (2012). Chem. Heterocycl., Comp. 48, 931.
30. Khalafy J, Ezzati M, Rimaz M, Poursattar Marjani A, Yaghoobnejad Asl H. (2014) J. Iran. Chem. Soc. 11, 1067.
31. Khalafy J, Etivand N, Dilmaghani S, Ezzati M, A. Poursattar Marjani (2014). Tetrahedron Lett. 55, 3781.
32. Hitchings G. H, Elion G. B, Wanderers H and Falco E. A (1948). Biol. Chem.174, 765.
33. Futterman S (1957). Biol. Chem. 228, 1031.

34. Cheng C. C and Roth B (1982). In Progress in Medicinal Chem., (eds Ellis GP and West GB), Butterworths London. 19, 267.
35. Kompis I, Wick A, Chim (1977). Acta. 60, 3025.
36. Polak A, Scholer H. J (1975). Chemotherapy. 21, 113.
37. Padamshari B, Vaidya V. P and Vijayayakumar M. L (2002). Indian J. Hetero. Chem. 12, 89-94.
38. Naik T. A and Chikhalia K. H (2007). E-Journal of Chem. 4, 1, 60-66.
39. Aly and A. A (2005). Chinese J. of Chem. 23, 211-217.
40. Mogilaiah K, Sudhakar G. R (2003). Indian J. Chem. 42B, 636-640.
41. Mishra A, Singh D. V (2004). Indian J. Hetero. Chem. 14, 43-46.
42. Alagarsamy V, Pathak U. S, Rajasolomon V, Meena S, Ramseshu K. V, Rajesh R(2004). Indian J. Hetero. Chem. 13, 347.
43. Vyas R, Udaibhan Gahlot S, Verma B. L (2003). Indian J. Hetero. Chem. 13, 115.
44. Callery P and Gannett P (2002).Cancer and Cancer Chemotherapy: In Foye's Principles of Medicinal Chemistry (eds Williams D. A and Lemke T. L), Lippincott Williams and Wilkins, Philadelphia. 934–935.
45. Omar N. Al Safarjalani, Reem Rais, Junxing Shi, Raymond F. Schinazi, Fardos N. M. Naguib, Mahmoud H. el Kouni (2005). Cancer Chemotherapy Pharmacology. 55, 541–551.
46. Singh P, Kaur J and Paul K (2008). Indian J. Chem. 47B, 291-296.
47. Pedeboscq S, Gravier D, Casadebaig F, Hou G, Gissot A, Giorgi F. D, Ichas F, Cambar J, Pometan J(2010). Eur. J. Med. Chem. 45, 2473-2479.
48. Fathalla O. A, Zeid I. F, Haiba M. E, Soliman A. M, Abd-Elmoez and E. L Serwy W. S(2009). World J. Chem. 4, 2, 127-132.
49. Talal A, Allaf K. A and Redna I (1996). Applied Organo-metallic Chem.10, 47.
50. Malic S, Grdisab M, Pavelicb K, Mintasa M (1999). J. Med. Chem. 34, 405−413.
51. J. H. Burchenal, M. L. Murphy, R. R. Ellison, M. P. Sykes, T. C. Tan, l. A. Leone, D. A. Karnof-sky, l. F. Craver, H. W. Dargeon and C. P. Rhoads(1953). Blood. 8, 965-999.
52. Giller S. A, Zhuk R. A and Lidak M. I. U (1967). Akad. Nauk SSR. 176(2), 332-335.
53. Remers W. A (1998). Antineoplastic Agents: In Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry (eds Delgado J. N and Remers W. A), Lippincott Williams and Wilkins, Philadelphia. 366–368.
54. Weller M, Muller B, Koch R, Bamberg M and Krauseneck P (2003). Clin. Oncol. 21, 3276–3284.
55. Kennedy B. J, Torkelson J. L, Torlakovic E (1999). Cancer. 85, 2265–2272.
56. Horton T. M, Blaney S. M, Langevin A. M, Kuhn J. G, Kamen B, Berg S. L, Weitman S(2005). Cancer Res. 11, 1884–1889.
57. Fu R. G, You Q. D, Yang L , Wu W. T, Jiang C, Xu X. L(2010). Bioorg Med Chem. 18, 22, 8035-8043.
58. Kim D. C, Lee Y. R, Yang B. S, Shin K. J, Kim D. J, Chung B Y(2003). Eur J Med Chem. 38, 5, 525-532.
59. Schenone S, Bruno O, Bondavalli F, Ranise A, Mosti L, Menozzi G (2004). Eur J Med Chem. 39, 11, 939-946.
60. Abignente E, Sacchi A, Laneri S, Rossi F, D'Amico M, Berrino L, Calderaro V, Parrillo C(1994). Eur J Med Chem. 29, 4, 279-286
61. Kosaku Hirota , Mitsuomi Shirahashi , Shigeo Senda , Motoi Yogo(1990). J. Hetero. Chem. 27, 717.
62. Bruno Kokel, J. Guillaumel, R. Royer (1994). J. Hetero. Chem. 31, 1185.
63. Salvador, Javier Alonso, Juan A. Diaz, Francisco Junquera (1990). J. Hetero. Chem. 27, 269.
64. Nazario Martín, Margarita Quinteiro , Carlos Seoane , Jose L Soto (1997). J. Hetero. Chem. 34, 957.
65. Benjamin Podanyi, G. Rabloczky , M. Kurthy, Péter Mátyus, Nándor Makk, Anikó Tegdes, Judit Kosáry, Endre Kasztreiner (1990). J. Hetero. Chem. 27, 2, 151-155.

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