Academic Sciences

Asian Journal of Pharmaceutical and Clinical Research

Vol. 4, Issue 4, 2011 ISSN - 0974-2441

Review Article

PYRIDINE" A VERSATILE NUCLEUSE IN PHARMACEUTICAL FIELD

AJIT CHAUBEY*, S.N.PANDEYA

Department of Pharmaceutical Sciences, Saroj Institute of Technology & Management, Sultanpur Road, Lucknow, 226002
Email: chaubeyajit80@gmail.com

Received: 28 June 2011, Revised and Accepted: 18 July 2011

ABSTRACT

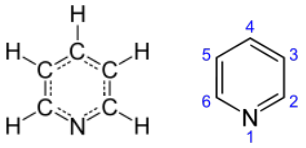
The pyridine is found to have a large no. of biological activities those including antiviral, anticancer, antimicrobial, antidiabetic, antitubercular etc. In this review we have reported some newer biological activities such as antidote, antileishmanial, antioxidant & antichagasic, antithrombin , anticoagulant etc along with most of the traditional biological activities. Pyridine is also a very active neutraceutical found in the form of vitamin B3 i.e Pyridoxine

Keywords: Pyridine, Pyridoxine, Antiviral, Anticancer, Antialzheimer

INTRODUCTION

Pyridine is a heterocyclic organic compound with the chemical formula C_5H_5N. It is structurally related to benzene, with one CH group replaced by a nitrogen atom. It is used as a precursor to agrochemicals and pharmaceuticals and is also an important solvent and reagsent.[1] Pyridine was first isolated and characterized by Anderson in 1846. It was obtained from bone oil and from coal tar. The cyclic nature of pyridine was recognized by Korner and Dewar in 1869.[2] It plays a key role catalyzing both biological and chemical systems. In many enzymes of living organisms it is the prosthetic pyridine nucleotide (NADP) that is involved in various oxidation–reduction processes. Other evidence of the potent activity of pyridine in biological systems is its presence in the important vitamins niacin and pyridoxine (vitamin B6) and also in highly toxic alkaloids such as nicotine. In the pharmaceutical industry, pyridine forms the nucleus of over 7000 existing drugs. Pyridine ring system is very widely distributed in nature, especially in plant kingdom. Many important alkaloids atropine from Atropa belladonna, Deadly nightshade, contains saturated pyridine nucleus. in ancient times woman have used the fluid of leaves of the deadly nightshade to dilate pupils of eyes (mydriatic properties).[3]

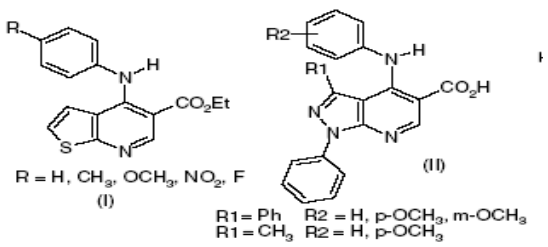
Pyridine



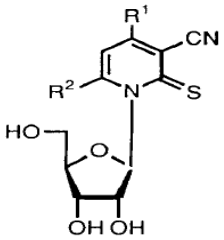
Biological Activities

Antiviral activity

- Bernardino *et al* synthesized new 4-(phenylamino)thieno[2,3-b]pyridine derivatives [(1)], which showed inhibitory activity against Herpes simplex virus type 1 (HSV-1). Structure–activity relationships (SAR) of these compounds in comparison to the derivatives 4-(phenylamino)-1H-pyrazolo [3,4-b]pyridine that show several different biological activities, such as anti-HIV-1 and -Vacci´nia virus.[4]

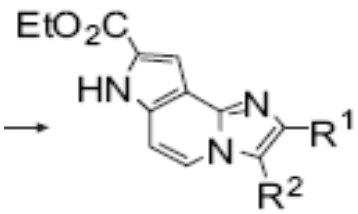


- Attia *et al* synthesized some pyridine ribosides, used for the treatment of HIV infection diseases. The 1-(β-D-ribofuranosyl)-pyridine-2-thiones (2) were found to be most active anti- HIV agents.[5]



$R^1 = C_6H_5$, $R^2 = 4\text{-}ClC_6H_4$ (2)

- Chezal *et al* synthesized an imidazo [1,2-a]pyrrolo [2,3-c] pyridine series [(3)], which are active against classical swine fever virus (CSFV) and the border disease virus (BDV) to the genus Pestivirus. Pestiviruses cause important diseases of livestock such as bovine viral diarrhea in cattle classical swine fever in pigs and border disease in sheep.[6]

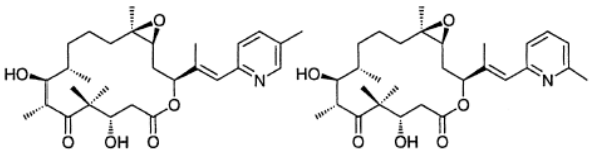


R^1 = Me, R^2 = H
R^1 = Ph, R^2 = H
R^1 = *m*-MeOPh, R^2 = H
R^1 = CF_3, R^2 = H
R^1 = *i*-Pr, R^2 = H
R^1 = *t*-Bu, R^2 = H
R^1 = H, R^2 = Br
R^1 = Me, R^2 = Br
R^1 = Me, R^2 = NO_2

(3)

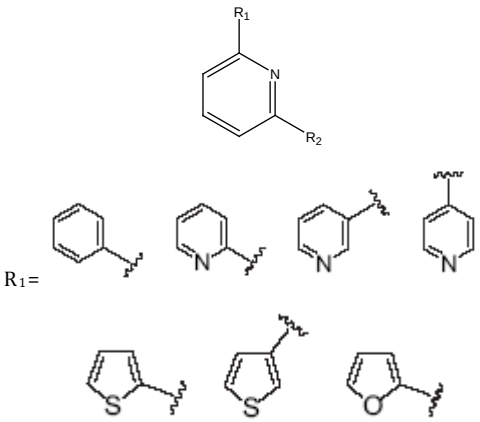
Anticancer activity

- Nicolaou *et al* synthesized pyridine epothilones [(4)] exhibiting cytotoxic properties against a number of human cancer cell lines. The compounds showed the importance of nitrogen atom at ortho position with the effect of methyl substitution on pyridine ring at 4- or 5- positions. [7]



(4)

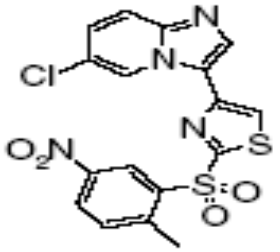
- Jong-Keun Son *et al* synthesized 2,6-diaryl-substituted pyridines [5] having cytotoxicity against several human cancer cell lines. It has the cytotoxicity and topoisomerase I inhibitory activity also.[8]



R_1 =

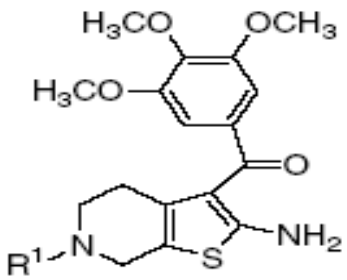
R_2 = (5)

- Hayakawa *et al* synthesized imidazo[1,2-a]pyridine derivatives. In a series of imidazo[1,2-a]pyridine compounds [6] the thiazole derivative showed potent p110a inhibitory activity and strong selectivity for p110a over other PI3K isoforms. Compound also inhibited tumor cell growth both in vitro and in vivo, suggesting that PI3K p110a is a potential target in cancer treatment.[9]



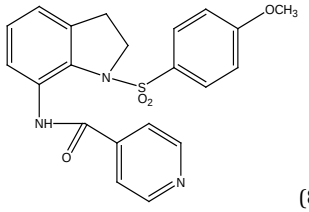
(6)

- Romagnoli *et al* synthesized 2-amino-3-(3',4',5'-trimethoxybenzoyl)- 6-substituted-4,5,6,7-tetrahydrothieno [2,3-c]pyridine derivatives [7] and evaluated against a panel of four cancer cell lines, and interacts strongly with tubulin by binding to the colchicine site. The compounds showed promising antiprolifirative activity,inhibition of tublin polymerization & cell cycle effect.[10]



R^1=CH_3, C_2H_5, n-C_3H_7, $CH_2C_6H_5$, $COCH_3$, $COOCH_3$ (7)

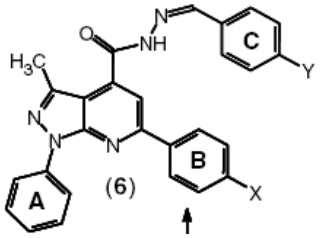
- Liou *et al* synthesized a novel oral indoline-sulfonamide agent [8], exhibiting potent activity against human cancer cells *in vitro* and *in vivo* through the disruption of microtubule.[11]



(8)

Antichagasic activity

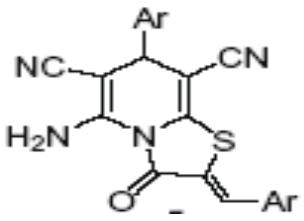
- Chagas' disease is caused by Trypanosoma cruzi, a parasite with a large zoonotic reservoir in Central and South America.1–3 Its endemy keeps 100 million people at risk and about 20 million people chronically infected with T. cruzi. Dias *et al* synthesized 1H-pyrazolo[3,4-b]pyridine series compounds[9] having antichagasic activity.[12]



(6) *(9)*

Antioxidant activity

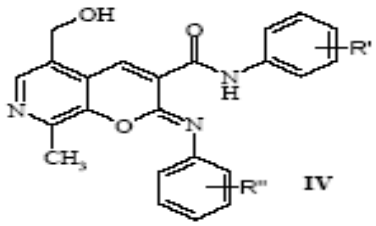
- Feng Shi *et al* synthesized thiazolo[3,2-a]pyridine derivatives [10] ,which scavenge free radicals.[13]



(10)

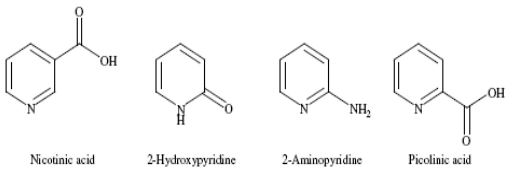
Antibacterial activity

- Ivachtchenko *et al* synthesized several novel 2-imino-5-hydroxymethyl-8-methyl-2H-pyrano[2,3-c]pyridine-3-(N-aryl) carboxamides [11] and evaluated for antibacterial and antifungal activities. Most of the compounds showed significant activity against bacterial or fungal strains (MIC in the range of 12.5–25 lg/mL), displaying better efficacy than the standard drugs.[14]



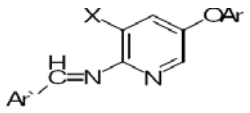
(11)

- Suksrichavalit *et al* prepared the Copper complexes of pyridine derivatives [12] and tested for their superoxide scavenging and antimicrobial activities. The copper complexes exerted SOD activity in the range of 49.07–130.23 mM. Particularly, copper complex of nicotinic acid with 2-hydroxypyridine was the most potent SOD mimic with an IC50 of 49.07 mM.[15]



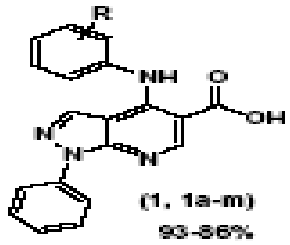
Nicotinic acid 2-Hydroxypyridine 2-Aminopyridine Picolinic acid (12)

- Bhatia *et al* synthesized a series of 5-substituted (arylmethylene) pyridin-2-amine [13] by condensing various 5-substituted pyridyl-2-amines with various aromatic aldehydes. All the compounds were screened for their antibacterial activities. QSAR equation reveled that selected electronic, steric and liphophillic parameters have correlation with antibacterial activity.[16]



(13)

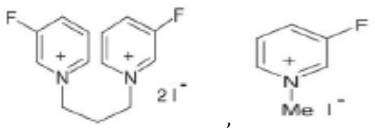
- B. Leal *et al* carried out the biological and theoretical evaluations of a 4-(arylamino)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acids series [14] and revealed that the 1H-pyrazolo[3,4-b]pyridine derivatives have significant antibacterial activity against a drug-resistant S. epidermidis clinical strain The (MIC) of the active derivatives against S. epidermidis was similar to that of oxacillin and twofold better than chloramphenicol.[17]



(14)

Antidote activity

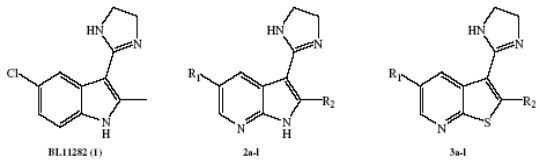
- M. Timperley *et al* synthesized some mono- and bis-quaternary pyridine salts [15] and evaluated their potential use in the treatment of organophosphorus nerve agent poisoning.[18]



(15)

Antidiabetic activity

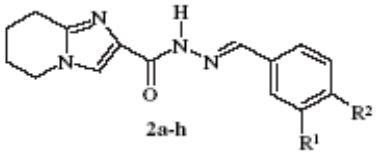
- Bahekar *et al* synthesized two series of 2,5-disubstituted-3-imidazol-2-yl-pyrrolo[2,3-b]pyridines thieno[2,3-b]pyridines [16]. The in vitro glucose dependent insulinotropic activity of all the test compounds was evaluated using RIN5F cell based assay and all the test compounds showed glucose and concentration dependent insulin secretion.[19]



(19)

Antifungal activity

- Ozdemir *et al* synthesized and evaluated the selective antifungal activity of 5,6,7,8-tetrahydroimidazo[1,2-a]pyridine derivatives. Eight new tetrahydroimidazo[1,2-a]pyridine derivatives [20] were synthesized and screened for their antifungal effects against a panel of ten human pathogenic Candida species using agar diffusion and broth microdilution assays, respectively. Among the analogues, the compound 5,6,7,8-tetrahydroimidazo[1,2-a]pyridine- 2-carboxylic acid-(4-cyanobenzylidene) showed very strong inhibitory activity (up to MIC 0.016 mg/mL) against the screened Candida species.[20]



CONCLUSION

As the biological activities of pyridine derivatives are shown above, the pyridine is found to be a very versatile nucleus in the pharmaceutical field. The derivatives are very much used as anticancer, antimicrobial, antiviral, antidiabetic & antithrombic agents etc. Thus the pyridine nucleus could be considered as the panacea for the management of various diseases.

ACKNOWLEDGEMENT

Authors are very much thankful to librarian CDRI , Lucknow to allow us to complete the latest literature.

REFERENCES

1. http//en.wikipedia.org/wiki/pyridine.
2. Pandeya S.N.,'A text book of pharmaceutical organic chemistry (heterocyclic and biomolecules) vol. 2nd, edition 1st,**2003**, by SG publisher, varansi, page no. 108-113.
3. Henry Gavin D.,De Novo synthesis of substituted pyridines;Tetrahedron 60, 2004, 6043-606.
4. Alice Maria Rolim Bernardino, Helena Carla Castro,et al; "Design, synthesis, SAR, and biological evaluation of new 4-(phenylamino)thieno[2,3-b]pyridine derivatives", Bioorganic & Medicinal Chemistry 14 ,2006, 5765–5770.
5. Adel M. Attia and Hanaa A. Mansour, "synthesis of some pyfudine ribosides and their biological activity", Nucleosides & Nucleotides, 1999,18(l0), 2301-2306.
6. Jean-Michel Chezal ,"synthesis and antiviral activity of an imidazo[1,2-a]pyrrolo[2,3-c]pyridine series against the bovine viral diarrhea virus", European Journal of Medicinal Chemistry 45 ,2010,2044–2047.
7. KC Nicolaou ,"Chemical synthesis and biological properties of pyridine epothilones, Chemistry & Biology" 2000, 7:593-599.
8. Jong-Keun Son , Eung-Seok Lee,Synthesis of 2,6-diaryl-substituted pyridines and their antitumor activities, European Journal of Medicinal Chemistry 43, 2008 , 675-682.
9. Masahiko Hayakawa, Peter Parker and Paul Workman, Bioorganic & Medicinal Chemistry 15, 2007 ,403–412.
10. Romeo Romagnoli , "Synthesis and biological evaluation of 2-amino-3-(30,40,50-trimethoxybenzoyl)-6-substituted-4,5,6,7 tetrahydrothieno[2,3-c]pyridine derivativesas antimitotic agents and inhibitors of tubulin polymerization", Bioorganic & Medicinal Chemistry Letters 18 ,2008, 5041–5045.
11. Jing-Ping Liou, Kuo-Shun Hsu, Ching-Chuan Kuo, Chi-Yen Chang, Jang-Yang Chang, " A novel oral indoline-sulfonamide agent, J30, exhibits potent activity against human cancer cells *in vitro* and *in vivo* through the disruption of microtubule", JPET ,July 27, 2007 as DOI: 10.1124/jpet.107.126680.
12. Luiza R. S. Dias, "Synthesis, in vitro evaluation, and SAR studies of a potential antichagasic 1H-pyrazolo[3,4-b]pyridine series", Bioorganic & Medicinal Chemistry 15 ,2007, 211–219.
13. Feng Shi, SSNing Ma, "Green chemoselective synthesis of thiazolo[3,2-a]pyridine derivatives and evaluation of their antioxidant and cytotoxic activities", Bioorganic & Medicinal Chemistry Letters 19 ,2009, 5565–5568.
14. Alexandre V. Ivachtchenko , Sergiy M. Kovalenko, "Synthesis and antimicrobial activity of 5-hydroxymethyl-8-methyl-2-(N-arylimino)-pyrano[2,3-c]pyridine-3-(N-aryl)carboxamides", Bioorganic & Medicinal Chemistry Letters 15 (2005) 5483–5487.
15. T. Suksrichavalit , European Journal of Medicinal Chemistry 44 (2009) 3259–3265.
16. Bhatia M.S, "Synthesis and QSAR analysis of 5-substituted (arylmethylene)pyridin-2-amine derivatives as potential antibacterials", International Journal of Drug Discovery, ISSN: 0975–4423, Volume 1, Issue 1, 2009, pp-1-9.

17. Bruno Leal, Carlos R. Rodrigues, "Antibacterial profile against drug-resistant Staphylococcus epidermidis clinical strain and structure–activity relationship studies of 1H-pyrazolo[3,4-b]pyridine and thieno[2,3-b]pyridine derivatives", Bioorganic & Medicinal Chemistry 16 (2008) 8196–8204.
18. Christopher M. Timperley , Mike Bird, Suzannah C. Heard, Stuart Notman,Robert W. Read, John E.H. Tattersall, Simon R. Turner, Journal of Fluorine Chemistry 126 (2005) 1160–1165.
19. Rajesh H. Bahekar, Mukul R. Jain, Pradip A. Jadav, Vijay M. Prajapati, Dipam N. Patel, Arun A. Gupta, Ajay Sharma, Robby Tom, Debdutta Bandyopadhya,Honey Modi and Pankaj R. Patel, "Synthesis and antidiabetic activity of 2,5-disubstituted- 3-imidazol-2-yl-pyrrolo[2,3-b]pyridines and thieno[2,3-b]pyridines", Bioorganic & Medicinal Chemistry 15 (2007) 6782–6795.
20. Ahmet Ozdemir, Fatih Demirci, " synthesis and the selective antifungal activity of 5,6,7,8-tetrahydroimidazo[1,2-a]pyridine derivatives" E.journal of medicinal chemistery,45 ,2010,2080-2084.