Review Article

A Review on Six Membered Nitrogen Containing Heterocyclic Compounds with Various Biological Activities

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ABSTRACT

The heterocycles are currently considered as promising compounds for the development of novel therapeutic agents. The analogs of nitrogen-based heterocycles occupy an exclusive position as a valuable source of therapeutic agents in medicinal chemistry. More than 75% of drugs approved by the FDA and currently available in the market are nitrogen-containing heterocyclic moieties. In the forthcoming decade, a much greater share of new nitrogen-based pharmaceuticals is anticipated. Many new nitrogen-based heterocycles have been designed. The number of novel N-heterocyclic moieties with significant physiological properties and promising applications in medicinal chemistry is ever-growing. This paper aims to review on the pharmacological activities of six membered nitrogen contains heterocyclic compounds.

Keywords: Pyridine, Pyrimidine, Triazine, pharmacological activities.

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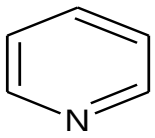
INTRODUCTION

Nitrogen-based heterocyclic chemistry is an important and unique class among the applied branches of organic chemistry, with a significant amount of research dedicated to the development of novel molecules and composites. These molecules have received increasing attention over the past two decades. They contributed to the development of numerous organic synthesis protocols and found abundant applications in the chemical sciences. . Among them six membered Nitrogen containing heterocyclic compounds in the wide range of medicinal chemistry such as antimicrobial, antitubercular, antiviral, anti-inflammatory, antibacterial, anti-obesity, antifungal, antihistaminic, anticancer, antihypertensive, and other potential medicinal agents with their broad applications in pathology and diagnostics. This review paper high light the six membered nitrogen containing heterocyclic compounds and some of the biological activities.

PYRIDINE

Pyridine is a basic heterocyclic organic compound with the chemical formula C5H5N. In many aspects it can be related to well established and very fundamental aromatic molecule, benzene, with one C-H group replaced by a nitrogen atom. Pyridine has a conjugated system of six π-electrons exactly as benzene has, that are delocalized over the heterocyclic ring. The molecule is planar in nature and follows Hückel criteria for aromaticity.



PYRIDINE
FIGURE 1

The name pyridine is derived from the Greek word and is the combination of two words "pyr" means fire and "idine" is used for aromatic bases. Nitrogen containing six membered aromatic pyridine and its derivatives abundantly exist in nature and they play a vital role in the field of heterocyclic chemistry. Such compounds are widely used for many applications in medicinal science[1]

PHARMACOLOGICAL ACTIVITY

1. Pyridine as Anticancer Activity

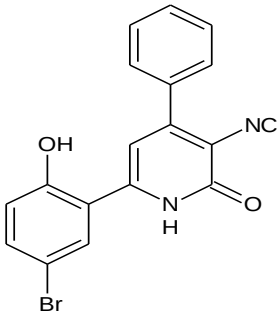


FIGURE 2

Ashraf H. Abadi *et al* synthesized series of 4,6-diaryl-2-imino-1,2-dihydropyridine-3-carbonitriles and exhibited good anticancer activity[2].

B. Narsaiah A *et al* synthesized series of novel nicotinohydrazide and 1,3,4-oxadiazol-2-yl)-6-(trifluoromethyl) pyridine derivatives and exhibited good anticancer activity[3].

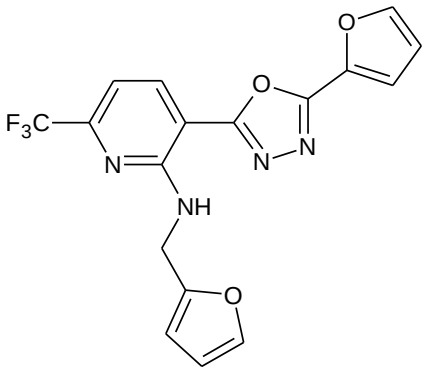


FIGURE 3

2. Pyridine as Antimicrobial Agent

Abd El-Galil E *et al* synthesized a series of chiral macrocyclic pyridines has been found good anti microbial activity[4].

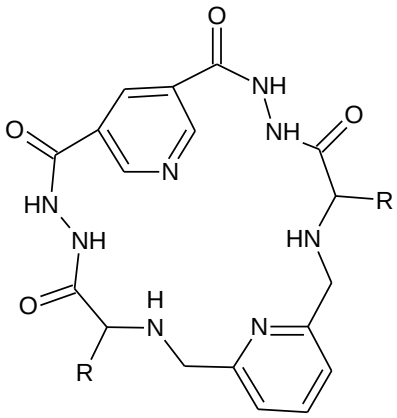


FIGURE 4

3. Pyridine as Antiviral Agent

Alain Gueiffier *et al* synthesized Imidazo[1,2-*a*]pyridines bearing a 3-(dithiolan-, dioxolan- or oxathiolan-2-yl) substituent and found to be good antiviral activity[5].

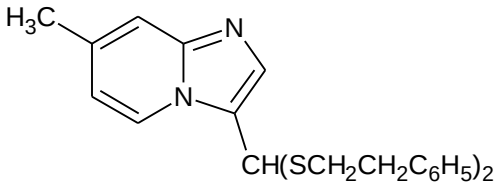


FIGURE 5

MARKETED FORMULATIONS

a. Etoricoxib

- Chemical formula – C18H15CIN2O2S
- Selective COX2 inhibitor
- Trade name of etoricoxib is Arcoxia

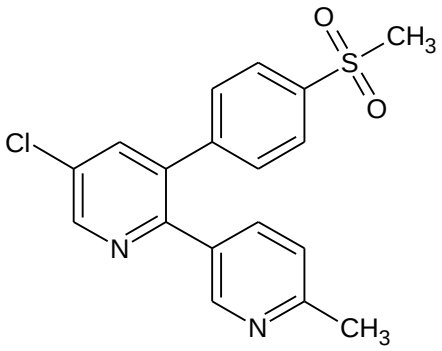


FIGURE 6

b. Perampanel

- Chemical formula C23H15N3O
- Antiepileptic drug used to treat partial seizures and generalized tonic - clonic seizures.
- Other names – E2007, Fycompa

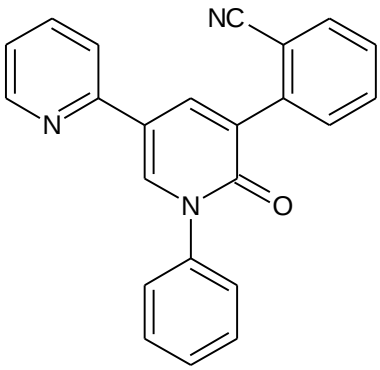
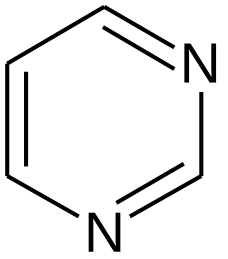


FIGURE 7

PYRIMIDINE

Pyrimidine is a heterocyclic aromatic organic compound similar to benzene and pyridine, containing two nitrogen atoms at positions 1 and 3 of the six-member ring. A pyrimidine has many properties in common with pyridine, as the number of nitrogen atoms in the ring increases the ring pi electrons become less energetic and electrophilic aromatic substitution gets more difficult while nucleophilic aromatic substitution gets easier.



PYRIMIDINE

FIGURE 8

Pyrimidine derivatives is a class of heterocyclic compound that have attracted significant interest in medicinal chemistry as they have a wide range of pharmaceutical and pharmacological applications such as antineoplastic, antiviral, antibacterial, expectorant, urinary tract infection, parkinsonism, anthelmintic, vasodilator, liver disorder, infections of the respiratory tract and ear, treatment of

gastrointestinal roundworms, peripheral neuropathies and disorders associated with hyperuricaemia[6].

1. Pyrimidine as Anti-Inflammatory Agent

Cottam *et al* were synthesized several pyrazolo[3,4-*d*] pyrimidine derivatives as potential inhibitor of adenosine kinase. One of the compound was found to display good anti-inflammatory activity[7].

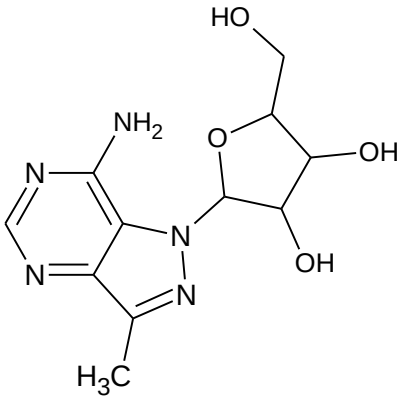


FIGURE 9

Sham M. Sondhi *et al* synthesized pyrimidine derivatives and have been found good anti-inflammatory activity [8].

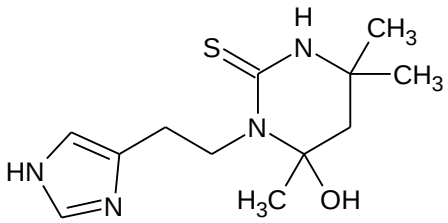


FIGURE 10

2. Pyrimidine as Anti Cancer Agent

Edwin Wager *et al* synthesized pyrimidine derivatives to study their cytotoxic activity. Some of the derivatives exhibit good anticancer activity[9].

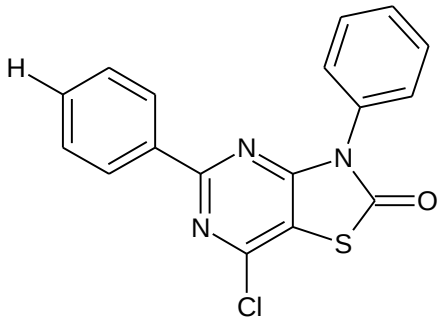


FIGURE 11

3. Pyrimidine as Anticonvulsant Agents

Li-Ping Guannovel *et al* synthesized a series of 7-substituted-[1,2,4]triazolo[4,3-*f*]pyrimidine derivatives was synthesized as potential anticonvulsant agents[10].

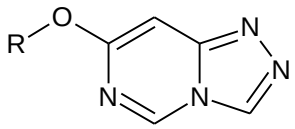


FIGURE 12

MARKETED FORMULATIONS

a) 5-FLUROURACIL

- CHEMICAL FORMULA – C4H3FN2O3
- Anti cancer drug used for colon cancer ,cervical cancer, esophageal cancer etc
- Brand name - Adrucil

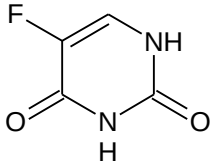


FIGURE 13

b) AFLOQUALONE

- CHEMICAL FORMULA – C16H14FN3O
- Sedative and muscle relaxant effect .
- Brand name – Airomate

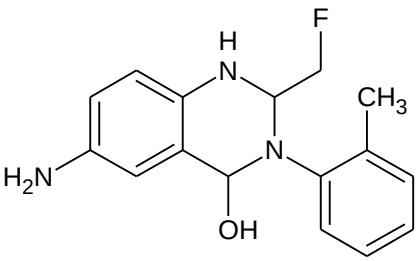
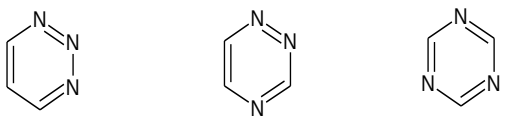


FIGURE 14

TRIAZINE

Triazines are a class of nitrogen-containing heterocycles. The parent molecules' molecular formula is $C_3H_3N_3$. They exist in three isomeric forms 1,2,3-triazine, 1,2,4-triazine, and 1,3,5-triazine (s-triazine). The isomers of triazine are distinguished from each other by the positions of their nitrogen atoms Compared to benzene, the resonance energy of triazines is very less, and hence less aromatic than benzene. 1,3,5-Triazine (s-triazine) has been widely used in organic reactions that offers access to a multitude of useful molecules due to its specific structure and electronic properties.



1,2,3-TRIAZINE 1,2,4-TRIAZINE 1,3,5-TRIAZINE

FIGURE 15

Generally, triazines play a vital role in many biological processes and synthetic drug chemistry. They constitute core structure in many chemotherapeutic agents, which includes anti-HIV, antibacterial, anti-angiogenesis, and antimalarial activities. In addition, the s-triazine ring

containing compounds have also found application in pesticides, resin intermediates, dyes and explosives[11].

PHARMACOLOGICAL ACTIVITY

1. Triazine as Antiviral Activity

Marcela Krecmerova *et al* synthesized Triazine Analogues of 1-(*S*)-[3-Hydroxy-2-(phosphonomethoxy)propyl] cytosine and was shown to exert strong activity against a broad spectrum of DNA viruses including adenoviruses, poxviruses, and herpes viruses[12].

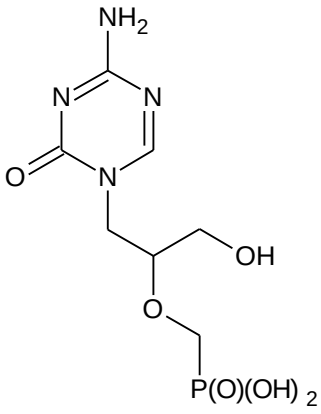


FIGURE 16

Kunihiro Sumot *et al* Synthesis Some 2,4,6-Trisubstituted 1,3,5-Triazines which showed a considerably high level of antiviral activity[13].

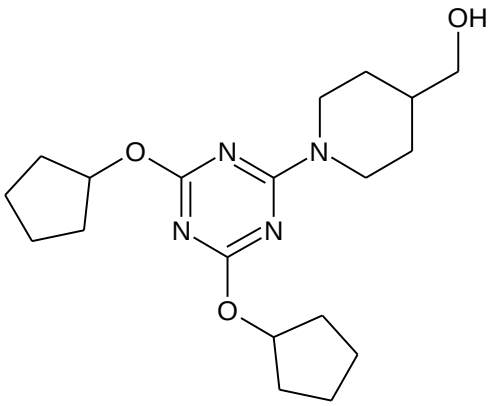


FIGURE 17

2. Triazine as Anti-Inflammatory Activity

Sepúlveda-Arias *et al* synthesized different derivatives and shows good anti-inflammatory activity[14].

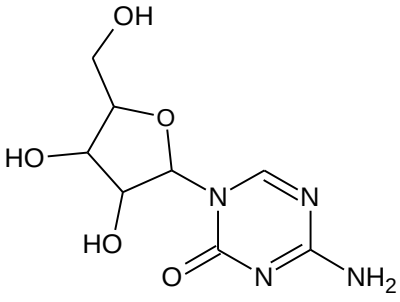


FIGURE 18

3. Triazine as Anticancer Activity

Kamaldeep Paul *et al* synthesized series of triazine-benzimidazole analogs has been designed and synthesized for their in vitro anticancer activities. Four compounds (6, 16, 17 and 20) were identified as highly potent anticancer agents against 60 human cancer cell lines with GI50 in the nanomolar range[15].

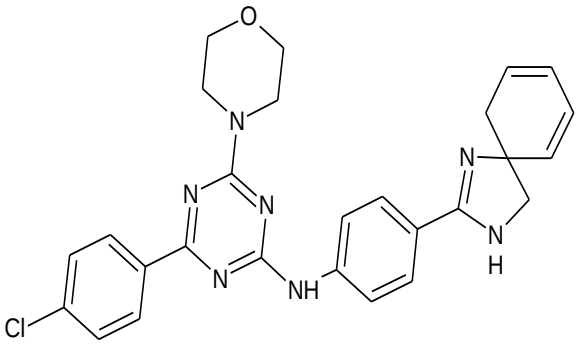


FIGURE 19

MARKETED FORMULATIONS

A. Lamotrigine

- CHEMICAL FORMULA – C9H7Cl2N5
- Anticonvulsant medication used to treat epilepsy.
- Brand name – Lamictal

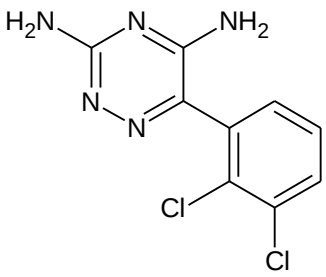


FIGURE 20

B. Tirapazamine

- CHEMICAL FORMULA – C7H6N4O2
- Experimental anticancer drug that is activated in hypoxic conditions.
- Other name – SR4233

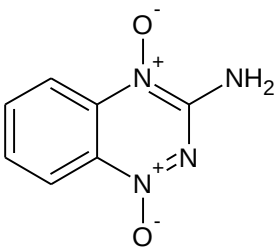


FIGURE 21

CONCLUSIONS

The scope of nitrogen-based compounds in medicine is growing daily and their diverse analogs provide a viable and important path for the discover of drugs with various biological applications. The N-heterocyclic frameworks offer a high degree of structural diversity that has proven

useful for the search of new therapeutic agents in improving the pharmacokinetics and other physicochemical features. Nitrogen containing six membered heterocyclic compounds have wide spectrum of applications in the pharmaceutical field which are pharmacologically and physiologically active and it is used in the treatment of various diseases. On the basis of various literature surveys these derivatives show various activities like anti-fungal, anti-bacterial, anti-inflammatory, analgesic, anti-cancer, anti-depressant, anti-viral and anti-tubercular. This paper reviewed some of the biological activities of these compounds. The possible improvements in the activity can be further achieved by slight modifications in the substituent's on the basic nucleus of these compounds. Thus, has been long focused for research interest in the field of medicine, due to excellent activities exhibited by its derivatives.

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