

# Biological Significance of Nitrogen Containing Heterocyclic compounds - A Mini Review

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## ABSTRACT

Heterocyclic compounds are present in abundance in our surroundings. They owe their importance in the biological system due to uniqueness in their structural skeleton. They are naturally found in nucleic acid, vitamins, antibiotics, hormones etc. Nitrogen containing heterocyclic compounds are an important class of heterocyclic compounds that has paid significant contribution towards medicinal chemistry. The types of compounds depend upon number of nitrogen atoms and their position. e.g. Pyrimidine contains one nitrogen atom in ring skeleton. With two nitrogen atoms it is called diazine, pyrazine etc. However, the review tends to focus on the importance of Pyrimidine class of compounds and their role as antibacterial, antifungal, anti-malarial, anticancer and other agents. The review also includes some of the marketed drugs having Pyrimidine ring nucleus and their application.

## Keywords

Heterocyclic compounds, Pyrimidine, anti-bacterial, antifungal, anti-malarial, anticancer.

## 1. INTRODUCTION

Pyrimidines are heterocyclic compounds similar to pyridine. Pyridine is a 6-membered cyclic compound that contains 4-carbon atoms and 2-nitrogen atoms at position 1 and 3<sup>(1)</sup>. Though, pyrimidine itself is not very active, its derivatives are very important in medicinal chemistry.

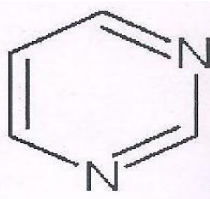


Fig. 1 Pyrimidine

Heterocyclic rings are important components of hormones, vitamins, amino acids and synthesized drugs. Pyrrole, thiophene, piperidine, furan, pyridine, pyrrolidine, thiazole etc. are very important heterocyclic compounds used in synthesis.<sup>(2)</sup>

Heterocyclic compounds with nitrogen have an important place in the medicinal chemistry. Azine, pyridine, diazine, pyrimidine, pyrazine are various examples of nitrogen containing heterocyclic compounds. Among all these compounds, pyrimidines are one of the most important categories of compounds owing their importance to pharmacological activities. It is one of the important components of all the cells in living beings<sup>(3)</sup>. Pyrimidines are also important components of nucleic acids, as a part of bases like thiamine, uracil and cytosine.<sup>(4)</sup>

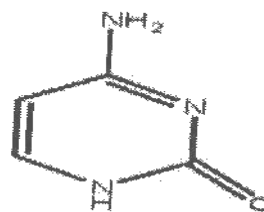


Fig. 2 Cytosine

Pyrimidine skeleton is present in vitamins, riboflavin, thiamine, and folic acid<sup>(5)</sup>.

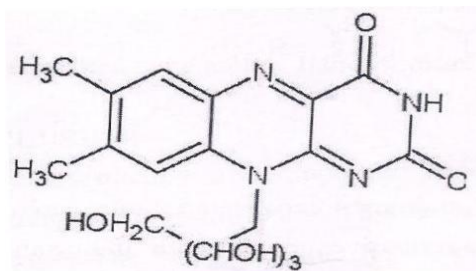


Fig.3 Riboflavin

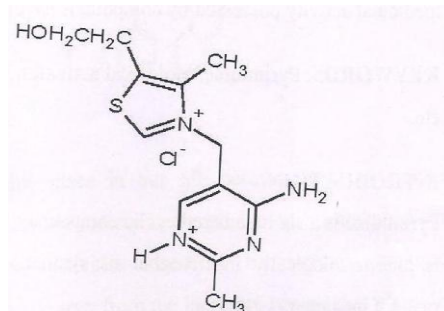


Fig. 4 Thiamine

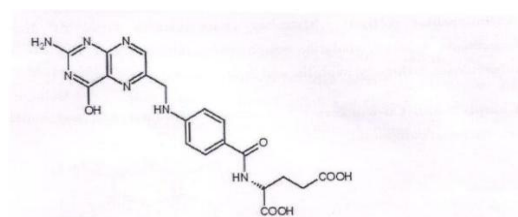
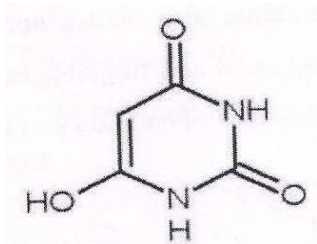
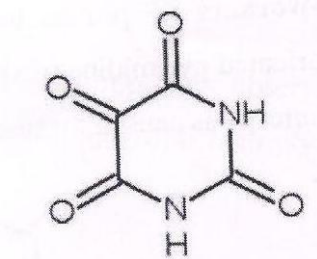


Fig. 5 Folic acid

Pyrimidine skeleton is present in many synthetic compounds such as barbituric acids and veranal, a derivative of barbituric acid that are used as hypnotics<sup>(6)</sup>.



**Fig. 6 Barbituric acid**

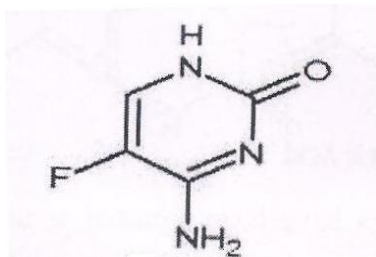


**Fig. 7 Veranal**

The presence of pyrimidine ring in bases of DNA and RNA is linked with their well-known biological activities. The literature survey indicated that the compounds containing pyrimidine nucleus exhibit pharmacological activities like anti-microbial<sup>(7)</sup>, anti-viral<sup>(8)</sup>, anti-tumor<sup>(9)</sup>, anti-malarial<sup>(10)</sup>, anti-neoplastic<sup>(11)</sup>, anti-HIV<sup>(12)</sup>, cardiovascular agents<sup>(13)</sup>, anti-fungal, anti-histaminic, anti-diabetic and herbicidal.

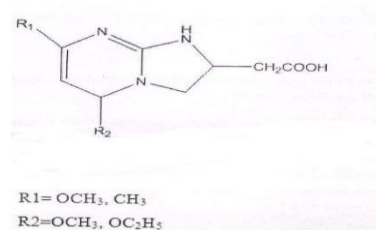
The drugs like sulphonamides, anti-tumor, barbiturates and anti-microbial agents also belong to series of pyrimidine based heterocyclic compounds.

Polak A. along with his co-workers<sup>(14)</sup>. Synthesized Flucytosine, and characterized its antifungal activities towards infections caused by strains of Cryptococcus and Candida.

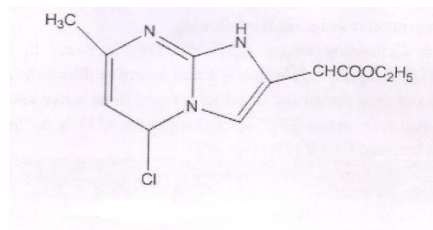


**Fig. 8 Flucytosine**

Sacchi & coworkers<sup>(15)</sup> prepared compounds (9) and (10) that showed anti-inflammatory activities

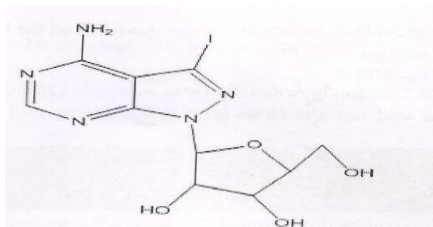


**Fig. 9**



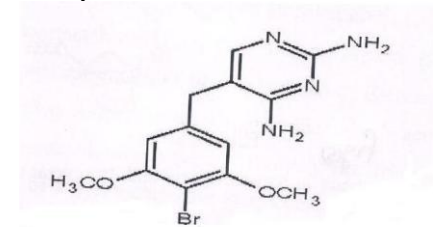
**Fig. 10**

Cottom & coworkers<sup>(16)</sup>. Reported the synthesis of (11) as inhibitor of adenosine kinase. The compound (11) is found to show anti-inflammatory properties.



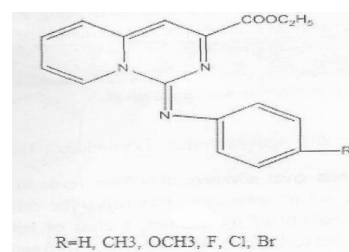
**Fig. 11**

Kompis I & et al<sup>(17)</sup> synthesized Brodimoprim (12). The important observation regarding this compound is that it is very effective in bacterial infections.

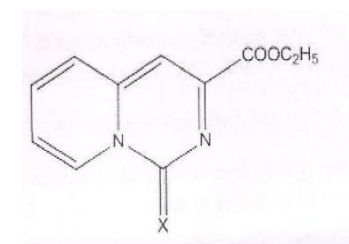


**Fig.12 Brodimoprim**

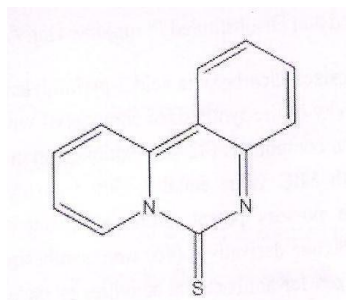
Molina & coworkers<sup>(18)</sup>. Synthesized a number of pyrido (1, 2-c) pyrimidine derivatives (13),(14) and (15) that showed their effects on leucocytes.



**Fig. 13**

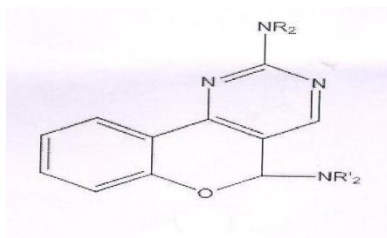


X = O, S **Fig. 14**



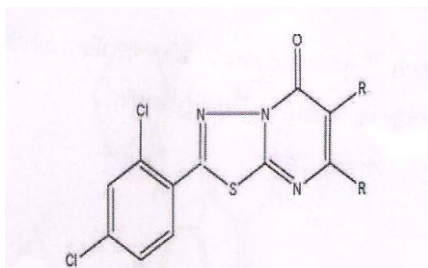
**Fig. 15**

The synthesis of 2, 5-cycloamino-5H, benzopyrano (4, 3-d) pyrimidines (16) by Bruno & coworkers<sup>(19)</sup> helped the medical fraternity to use its antiplatelet activity.



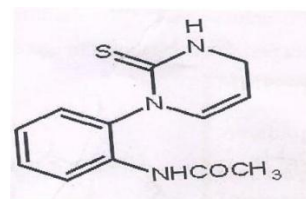
**Fig. 16**

Gogia and coworkers<sup>(20)</sup> synthesized 1, 3, 4-thiadizolo-(3, 2-a) pyrimidine-5-one (17). The compound has been found to exhibit antifungal properties.

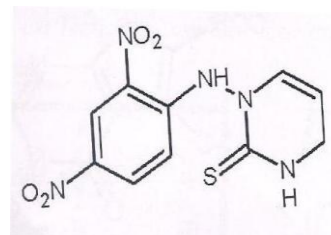


**Fig. 17**

Sondhi S.M. and coworkers<sup>(21)</sup> synthesized two pyrimidine derivatives (18, 19) & characterized their analgesic and anti-inflammatory properties.

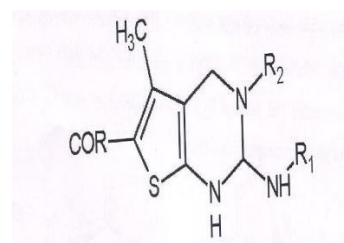


**Fig. 18**



**Fig. 19**

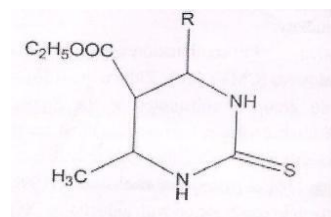
Rathod I.S. and coworkers<sup>(22)</sup> Synthesized derivatives of thieno (2, 3-d) pyrimidine-4(3H) - ones (20) and reported their analgesic activities.



R= -CH<sub>3</sub>, -NHPH R<sub>1</sub>=R<sub>2</sub>= Ph, o-Anisyl

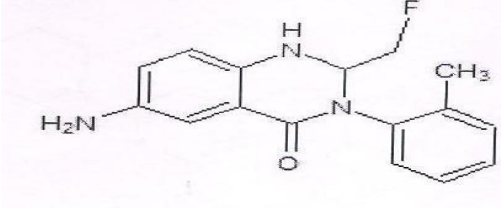
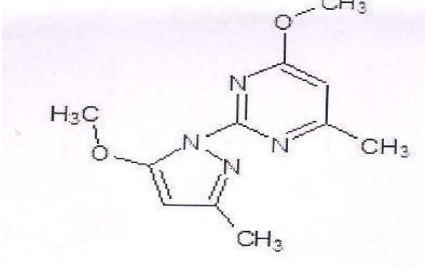
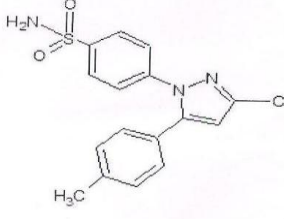
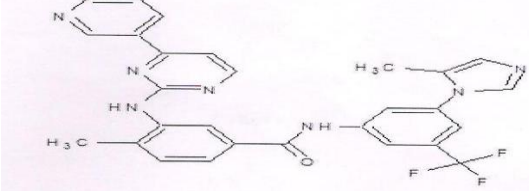
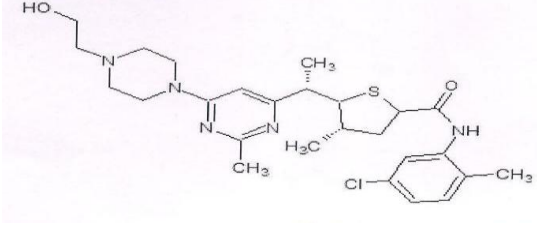
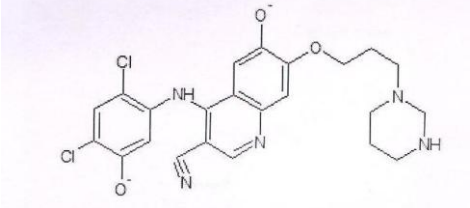
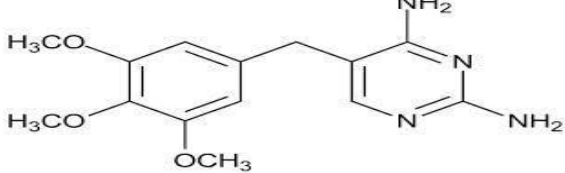
**Fig. 20**

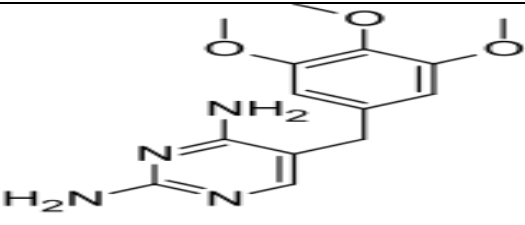
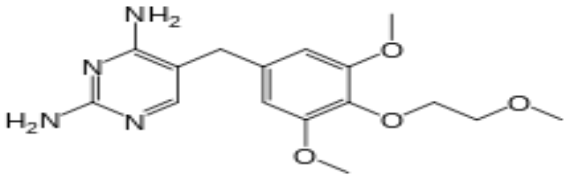
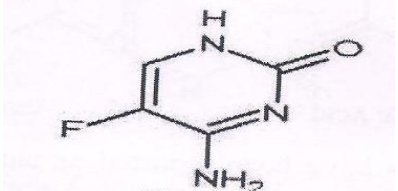
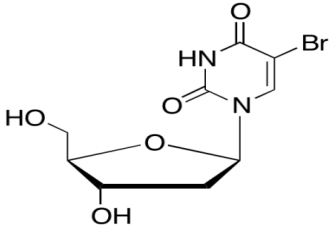
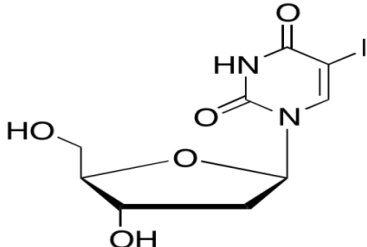
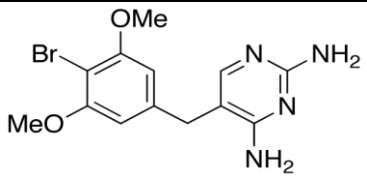
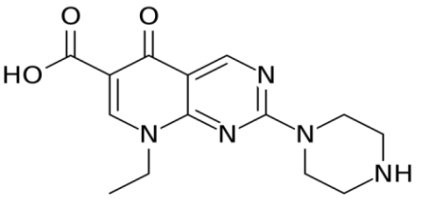
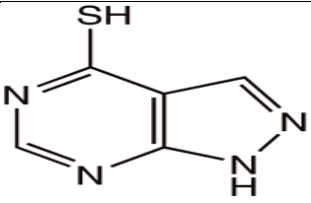
Gaby, Hamide and Gharab<sup>(23)</sup> prepared a series of pyrimidine -2-thione (21). Some of them showed anti- cancer properties.



**Fig. 21**

Marketed drugs containing Pyrimidines nucleus Skelton are listed below

Biological activity	Compound	Structure
Anti-inflammatory and Analgesics	Afloqualone	
	Epirizole	
	Celecoxib	
Anti-cancer	Nilotinib	
	Dasatinib	
	Bosutinib	
	Trimethoprim	

Anti-bacterial	Metiotrim	
	Tetroxoprim	
Anti-fungal	Flucytosine	
Anti-viral	Broxuridine	
	Idoxuridina	
Respiratory tract infections	Brodimoprim	
Urinary tract infections	Pipemidic acid	
Hyperuricaemia disorders	Tisopurine	

## 2. CONCLUSION

Pyrimidine is a unique heterocyclic compound found as a part of DNA & RNA & therefore it is one of the essential component of all the living cells. Besides this many natural compounds have been found to contain this important structural moiety. Pyrimidine has an important place in medicinal field because of its wide spectrum of pharmacological activities as reported in the reviewed article. Many of the researchers had already worked on it & had synthesized compounds with pyrimidines & fused pyrimidens ring skelton which are of great help to the medical paternity in curing & treating patients suffering from various ailments & many more are working on this unique moiety to further explore its activities to help the mankind by synthesizing new drugs.

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