



# A REVIEW ON MEDICINALLY IMPORTANT NITROGEN HETEROCYCLIC COMPOUNDS

**A.V.G.S.PRASAD & FALGUN PATEL**

R&D department Nandesari Drugs & Pharmaceuticals Pvt Ltd, 167-168 GIDC Industrial Estate, Nandesari, Vadodara, Gujarat 391340

## ABSTRACT:

Heterocyclic compounds are rapidly increasing in number due to extensive synthetic research and also their synthetic utility. Such compounds have a wide range of uses in the field of medicinal chemistry. According to prior research, more than 90% of medicines containing heterocyclic compounds have been developed after the obtainment of a thorough scientific grasp of the biological system. The present review article provides detailed information regarding nitrogen (N) heterocyclic compounds.

**Keywords:** Heterocyclic compounds, Biological activity, Anticancer, Antiviral, Anti-inflammatory.

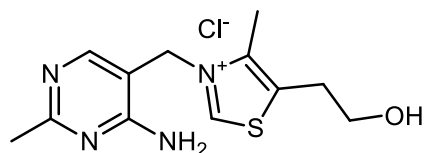
## 1. INTRODUCTION

Heterocyclic compounds, often known as heterocycles, are organic chemical compounds having a ring-like structure that includes one or more hetero atom. The most common heterocycles are those having three to ten membered rings and containing heteroatoms of nitrogen (N) ring-like structure that includes one or more heteroatoms. 59% of US FDA-approved drugs contain nitrogen heterocycles. The history of heterocyclic chemistry began in the 1800s, in step with the development of organic chemistry. <sup>\*1</sup>

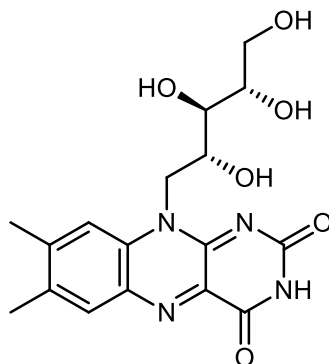
Statistically, more than 85% of all biologically active compounds are heterocycles or comprise a heterocycle and most frequently, nitrogen heterocycles as a backbone in their complex structures. These facts disclose and emphasize the vital role of heterocycles in modern drug design and drug discovery. <sup>\*2-4</sup>

Heterocyclic compounds, which are physiologically and pharmacologically active, have gained prominence in the medicinal study. Many biological compounds associated with living organisms, such as vitamins, hormones, and antibiotics, are composed of heterocyclic molecules. <sup>\*5</sup>

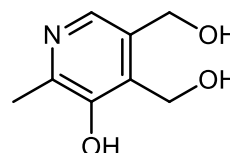
Furthermore, N-based heterocycles are indispensable diet components such as thiamin (vitamin B1), riboflavin (vitamin B2) and , pyridoxol (vitamin B6).<sup>\*6-8</sup>



thiamin (vitamin B1),



riboflavin (vitamin B2),



pyridoxol (vitamin B6),

Three and four-membered nitrogen heterocyclic compounds, because of their small size, are geometrically strained and thus readily opened; they are also readily formed.



Due to exhibiting diverse biological activities, nitrogen heterocyclic compounds have always been attractive targets to synthetic organic chemists.

In this review, we try to present a comprehensive overview of top prescribed drugs containing nitrogen heterocycles, describing their pharmacological properties, medical applications and their selected synthetic pathways.

## 2. MEDICINAL APPLICATIONS

Heterocyclic compounds play a key role in drug design due to their unique structural and electronic properties that allow them to interact with various receptors and enzymes in the body. As a result, the vast number of nitrogen heterocyclic compounds have been under continuous investigations from different points of view thus, found applications in pharmaceutical research and drug discovery.<sup>\*9-12</sup>

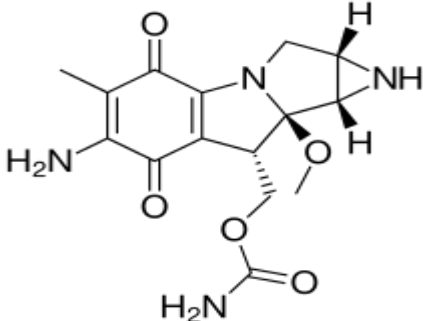
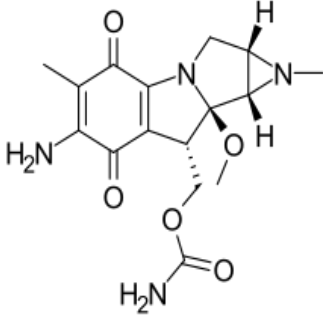
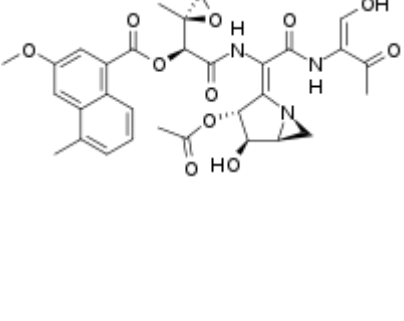
These interactions can lead to specific biological activities and therapeutic effects. In addition, the diverse chemical properties of heterocyclic compounds allow for the creation of compounds with unique pharmacological profiles that can help overcome limitations of existing drugs. Moreover, advances in computational and synthetic methods have enabled the rapid development and screening of new heterocyclic compounds for drug discovery.<sup>\*13</sup>

### THREE-MEMBERED RINGS

The three-membered ring heterocycles containing single atoms of nitrogen. Aziridine is a heterocyclic cyclopropane ring containing one nitrogen atom

Aziridine chemistry has since continued to advance with more powerful methods for both racemic and asymmetric syntheses and creative conversions of the resulting three-membered ring into valuable chiral amines and larger heterocycles. Aziridines are found in natural products and active pharmaceutical ingredients (APIs).<sup>\*14</sup>

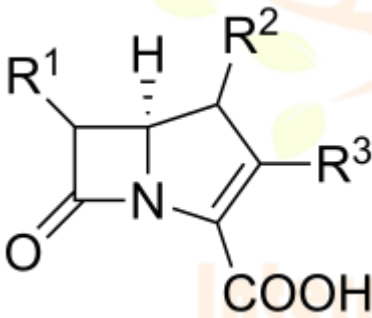
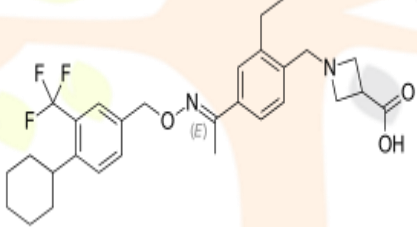
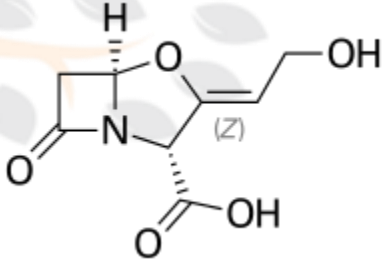
Many aziridine alkaloids have anticancer, antibacterial, and/or antimicrobial activity against selected cancer cell lines, pathogenic bacteria, and/or micro-organisms strongly indicating that the presence of the aziridine ring in natural as well as synthetic compounds is essential for such activities.

<b>MITOMYCIN</b> antitumor antibiotic	<b>PORFIROMYCIN</b> antineoplastic antibiotic	<b>AZINOMYCIN B</b> potent antitumor activity
		

## FOUR-MEMBERED RINGS

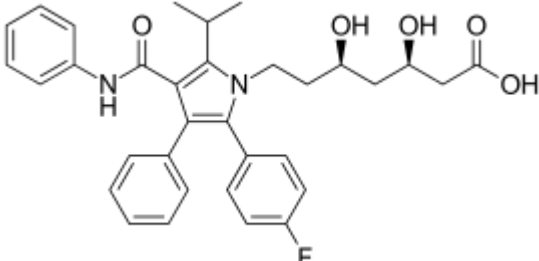
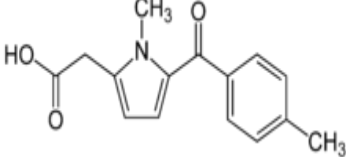
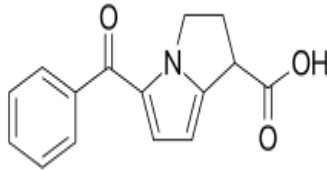
Azetidine is a fascinating four-membered nitrogen-containing heterocycle that is an analogue of cyclobutane

Compounds with the azetidine moiety display an important and diverse range of pharmacological activities, such as anticancer, antibacterial, antimicrobial, antischizophrenic, antimalarial, antiobesity, anti-inflammatory, antidiabetic, antiviral, antioxidant, analgesic, and dopamine antagonist activities, and are also useful for the treatment of central nervous system disorders and so forth.\*<sup>15</sup>

<b>CARBAPENEMS</b> antibiotic agents	<b>SIPONIMOD</b> To treat multiple sclerosis	<b>CLAVULANIC ACID</b> is a $\beta$ -lactam drug
		

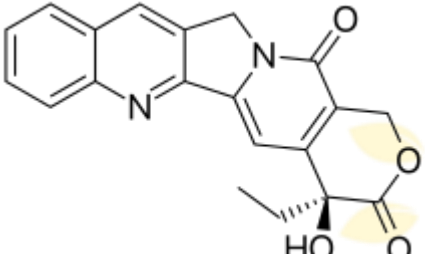
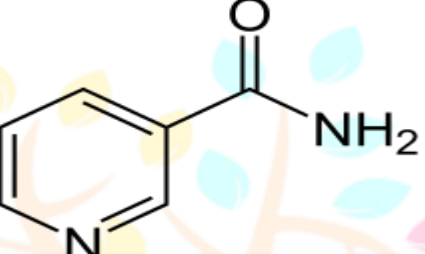
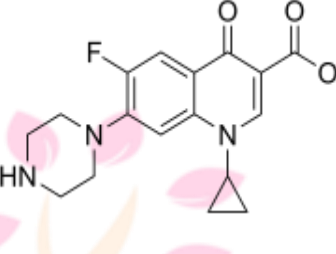
## FIVE MEMBERED RINGS

Pyrrole derivatives are nitrogen-containing five membered heterocyclic compounds and widely distributed in a large number of natural and non-natural compounds. These compounds possess a broad spectrum of biological activities such as anti-inflammatory, antiviral, antitumor, antifungal, and antibacterial activities.\*<sup>16</sup>

<b>ATORVASTATIN</b> to prevent cardiovascular disease	<b>TOLMETIN</b> non-steroidal anti-inflammatory drug	<b>KETOROLAC</b> Treat moderate-to-severe acute-onset pain.
		

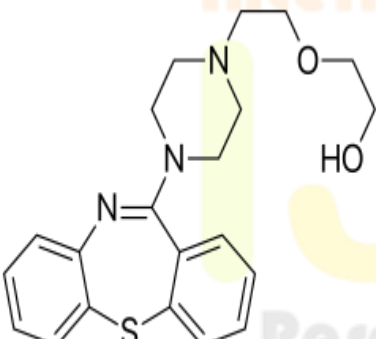
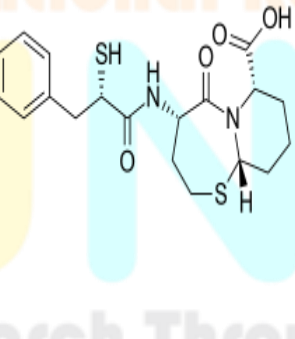
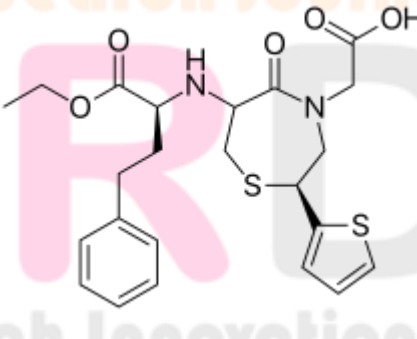
## SIX-MEMBERED RINGS

Six membered heterocycles containing nitrogen particularly pyridine derivatives are valuable compounds, particularly in medicinal chemistry. The structure of pyridine is analogous to that of benzene, with one of the carbons replaced by a nitrogen atom. Among them six membered Nitrogen containing heterocyclic compounds pyridine in the wide range of medicinal chemistry such as antimicrobial, ant tubercular, antiviral, anti-inflammatory, antibacterial, anti-obesity, antifungal, antihistaminic, anticancer, antihypertensive, and other potential medicinal agents with their broad applications in pathology and diagnostics. \*<sup>17</sup>

<b>CAMPTOTHECIN</b> Anticancer drugs.	<b>NICOTINAMIDE</b> water-soluble form of vitamin B3 or niacin	<b>CIPROFLOXACIN</b> antibiotic
		

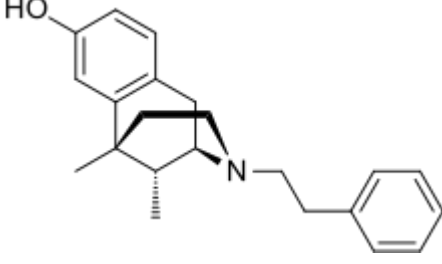
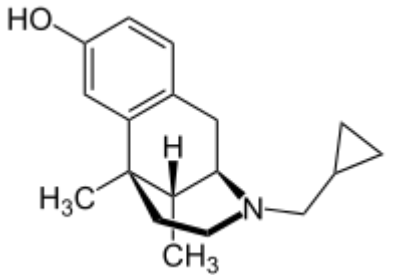
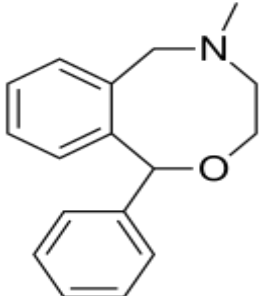
## SEVEN-MEMBERED RINGS

Azepine is a seven-membered nitrogen heterocycle with a biologically active epitope and a useful building block in the construction of various organic molecules. When a group or group of atoms is attached to the Azepine ring, where there are profound novel influences in the biological activity of these molecules. Azepine and its derivatives are imperative types of compounds that have been widely explored for the biological activities in the pharmaceutical industry. \*<sup>18</sup>

<b>QUETIAPINE</b> For schizophrenia and adjunctive treatment for major depressive disorder.	<b>OMAPATRILAT</b> antihypertensive agent	<b>TEMOCAPRIL</b> Is an ACE inhibitor.
		

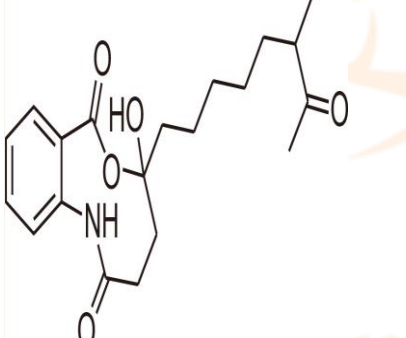
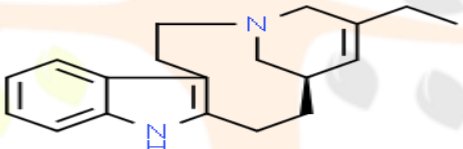
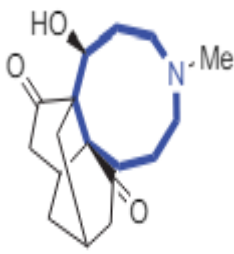
## EIGHT-MEMBERED RINGS

An eight membered Azocine ring play a pivotal role in the structures of various important natural products as well as precursors in the synthesis of biologically active compounds. Azocine derivatives have therapeutic application, such as antitussives, antihypertensives, analgesic, nasal decongestants, and anti-malaria.\*<sup>19</sup>

PHENAZOCINE opioid analgesic drug,	CYCLAZOCINE opioid analgesic drug,	NEFOPAM painkiller.
		

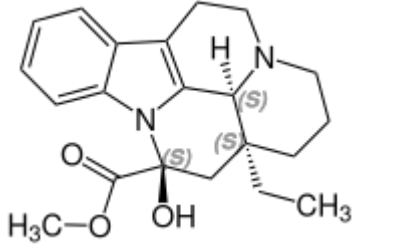
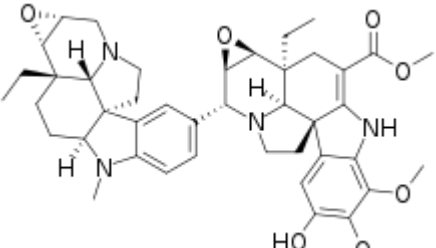
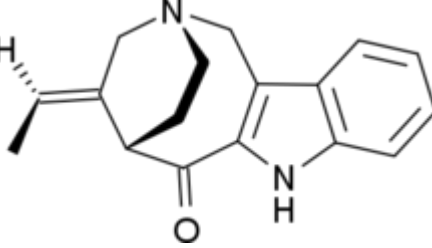
## NINE MEMBERED RINGS

Nine-membered nitrogen heterocyclic compounds are widely found in natural products and biologically active molecules.\*<sup>20</sup>

ANTAROIDE rhododendol treatment reduced the number of melanocytes in a pigmented 3D human skin model,	CLEAVAMINE Cholinergic agonists. It works by stimulating certain nerves to increase the amount of saliva you produce, making it easier	PALHININE A opioid analgesic drug,
		

## TEN MEMBERED RINGS

Ten -membered nitrogen heterocyclic compounds are widely found in natural products and biologically active molecules.\*<sup>21</sup>

VINCADINE It has a role as an antihypertensive agent, a vasodilator agent and a metabolite.	CONOFOLINE analgesic and pain killer	CONOLIDINE Analgesic and pain drug
		

## CONCLUSION

Nitrogen Heterocyclic compounds are one of the most significant types of organic molecules in medicinal chemistry and they are used as medications for various diseases. Numerous impressive accomplishments have shown that heterocyclic compounds have a wide range of therapeutic drug applications. Heterocyclic compounds are versatile synthetic targets and key structural units in organic synthesis and medicinal chemistry because of their exciting biological activities. The potential applications of heterocycles as anticancer, anti-inflammatory, antifungal, antibacterial, anti-Alzheimer's, antiviral, antidiabetic agents, etc., have attracted substantial interest within the pharmaceutical community. Interestingly, an increasing number of heterocycles have been identified as potential drug candidates in ongoing drug development.

## REFERENCES

1. Arora, P.; Arora, V.; Lamba, H.S.; Wadhwa, D: *Int. J. Pharma Sci.*, 2012, 3, 2947-2954
2. Renslo, A. R.; McKerrow, J. H. *Nat.Chem. Biol.*, 2006, 2, 701-10
3. T. Kunied, H. Mutsanga, *The chemistry of heterocyclic compounds*, Palmer, B, 2002,175
4. R. Gupta, M. Kumar; *Heterocyclic Chemistry*, 1996, 1, 98
5. J. Chabala, M. Miller. *Chemistry of Antiprotozoal Agents*, 1986, 25-85
6. Sriram K, Manzanares W, et al, *Nutr Clin Pract.* 2012 Feb; 27(1):41-50.
7. Oppenheimer SJ, Bull R, et al., *Med J.* 1983 Mar; 26(1):17-20.
8. Andon MB, Reynolds RD, et al., *Am J Clin Nutr.* 1989;50:1050–1058.
9. Nagaraju Kerru, Lalitha Gummidi, et al., *Nat. Rev. Drug Discov.* 2007; 6:881–890.
11. Smith B.R., Eastman C.M., Njardarson J.T.. *J. Med. Chem.* 2014; 57:9764–9773
12. Gordon E.M., Barrett R.W., Dower W.J., Fodor S.P.A., Gallop M.A. *J. Med. Chem.* 1994; 37:1385–1401
13. Walsh C.T. Nature loves nitrogen heterocycles. *Tetrahedron Lett.* 2015;56:3075–3081
14. Andleeb Amin et al., *Current Organic Chemistry* 25(16)July 202125(16)
15. Doraswamy K, Ramana PV (2013) *Chemical Science Transactions* 2(2): 649-655.
16. Mermer A, Keles T, Sirin Y.. *Bioorg Chem.* 2021;114:105076.
17. Ling Y., Hao et al., *Drug Design, Development and Therapy* . 2021;15:4289–4338.
18. Manvinder Kaur , Sonali Garg , et al.,\* *Current Organic Chemistry*, 2021, 25, 1-58
19. Stephanie Lee et al., *Bioorganic & Medicinal Chemistry* 202154(5):116560
20. A. J. Blake, I. A. Fallis, R. O. et al., *J. Chem. Soc., Chem. Commun.*, 1994, 2467.
21. J. B. Robert<sup>a</sup> and H. Weichmann<sup>b</sup> *J. Org. Chem.*, Vol. 43, No. 15, 1978 3031

Research Through Innovation