wjpmr, 2025, 11(1), 124-130

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

A REVIEW ON DIFFERENT FIVE MEMBERED NITROGENATED HETEROCYCLIC COMPOUNDS AND THEIR PHARMACEUTICAL ACTIVITIES

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Article Received on 24/10/2024 **Article Revised on 13/11/2024** **Article Accepted on 02/12/2024**

ABSTRACT

Five-membered nitrogenated heterocyclic compounds constitute a significant class of molecules with widespread applications in the pharmaceutical industry. This review briefly examines several key examples, including pyrroles, pyrazoles, imidazoles, and triazoles, highlighting their diverse pharmacological activities. These heterocycles serve as core structures in numerous drugs and drug candidates exhibiting anti-inflammatory, anti-cancer, anti-fungal, anti-viral, anti-hypertensive, and anti-ulcer properties, among others. The structural versatility of these scaffolds allows for the design and development of novel therapeutic agents targeting a broad range of diseases. While this overview provides a general introduction, the specific pharmacological profile of each compound is highly dependent on its substituents and overall molecular architecture.

KEYWORDS: - Five-membered heterocycles, nitrogenated heterocycles, pyrrole, pyrazole, imidazole, triazole, pharmaceutical activity.

INTRODUCTION

The largest families of organic compounds in organic chemistry belong to the heterocyclic compound family. Heterocyclic compounds are extremely important in our daily lives. These include five-membered nitrogen-containing heterocyclic compounds with a wide range of medicinal chemistry applications, including antimicrobial, antitubercular, antiviral, anti-inflammatory, antibacterial, anti-obesity, antiparasitic, antifungal, antihistaminic, anticancer, and antihypertensive drugs.[1]

All of the nitrogenous heterocyclic compounds with five members have a variety of uses in the pharmaceutical industry as well as other industries like agriculture. The chemistry and uses of a number of five-membered nitrogenous heterocyclic compounds and their derivatives that have been produced both lately and in the past are primarily highlighted in this review paper. Heterocyclic organic compounds are used in veterinary medicine, agrochemicals, medicines, optical brightening agents, corrosion inhibitors, antioxidants, and additives with a range of other uses. Moreover, many pigments and dyestuff were heterocyclic compounds. In order to advance biochemical research, they exhibit biological activities, such as antibacterial, antifungal, and anticancer properties. Heterocyclic compounds that include nitrogen have been shown to improve physical functioning capacity in cases of acute normobaric hypoxia, hypercapnia, hypothermia, and hyperthermia.[2]

Pyrrole: -pyrrole is a heterocyclic aromatic chemical compound having five members and the molecular formula C4H5N. It is a volatile, white liquid that quickly turns dark when exposed to air. Pyrrole is an essential part of more complex macromolecules, such as chlorins, heme porphyrins, and chlorophyll. It was initially discovered by F.F. Runge. As an ingredient in coal tar in 1834. Pyrrole derivatives are present in many biological components as natural products and co-factors. Common naturally occurring compounds that contain pyrrole include vitamin B12, bile pigments such as bilirubin and biliverdin, heme porphyrins, chlorophyll, bacteriochlorin, and porphyrinogens. E. Fischer created haemin in 1929, one of the earliest instances of a pyrrole-containing compound.[3] The vast majority of pharmacological structures contain pyrrole derivatives. Pyrrole derivatives have a variety of biological properties, such as tyrosine kinas inhibitors, antibacterial[4], cholesterol-lowering[5], antidiabetic[6],

antiviral[7], fungicidal[8], antiasthmatic[9], antioxidant[10], and antitubercular.[11]

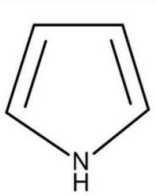


Fig.1: Pyrrole.

- **Structures and it's pharmacological activity**

1)Pyrrole with anti-cancer effect: - *iddum s.* synthesized a lamellarin O, lamellarin Q & lamellarin R analogues by Barton-Zard reaction which shows anti-cancer activity.[12]

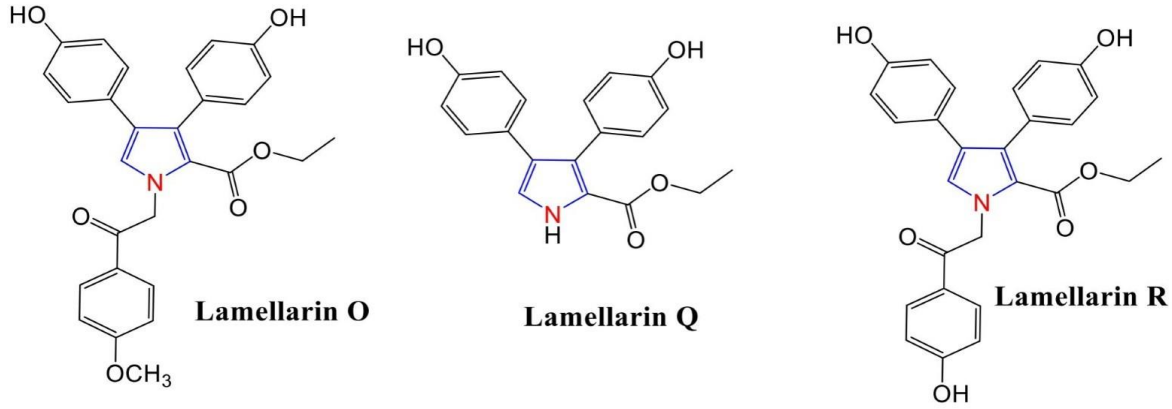


Fig. 2: Some Lamellarin Analogues.

2) Pyrrole with an antifungal activity: - pyrronitrin shows antifungal activity which is effective against superficial infections.[13]

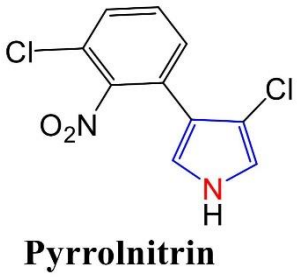


Fig.3

Imidazole: - Imidazole (1,3-diaza-2,4-cyclopentadiene) is a five-membered heterocyclic ring compound that is planar and contains three C and two N atoms in positions one and three. The formula for the molecule is C3H4N2. It dissolves in polar solvents like water. The molecule is known systemically as 1, 3 diazoles; one of the annular N atoms has a H atom and is therefore considered to be a pyrrole type N. There are two possible tautomeric forms for the hydrogen atom because it can be present on either of the two nitrogen atoms. A calculated dipole of 3.61D indicates that it is a highly polar compound that is completely soluble in water. The molecule's sextet of π-electrons—two from the protonated nitrogen atom and one from each of the other four atoms in the ring—makes it an aromatic compound. Imidazole can function as both an acid and a base since it is amphoteric. The proton that is acidic is located on N-1. N-3 is the fundamental site.[14]

The broad range of antimalarial, antibacterial, antifungal, anti-inflammatory, antiviral, antitubercular, and ultimately anticancer properties of imidazoles make them an extremely significant family of medication. Its activity is still being increased by the advancement of the imidazole moiety's synthesis and functionalisation at different positions.[15]

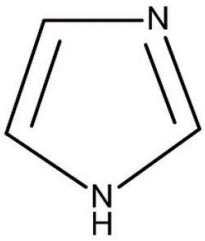


Fig. 4: Imidazole.

- **Structures and it's pharmacological activity**

1) Imidazole as anti-fungal and anti-bacterial activity: - *Daniele Zampieri et al.* synthesised derivatives of bis-imidazole and screened them for antifungal and antimycobacterial properties. Every compound exhibited moderate to good effectiveness against Candida glabrata and Candida albicans. Miconazole is used as a reference drug.[16]

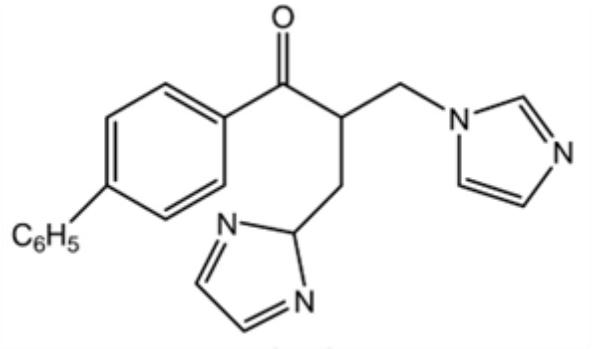
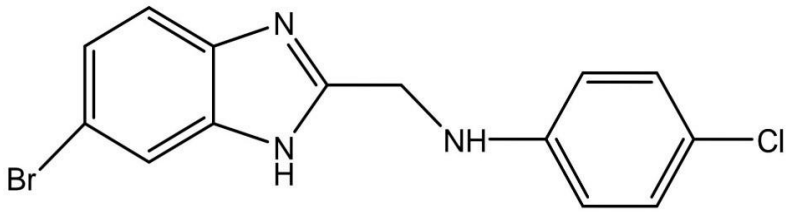


Fig. 5

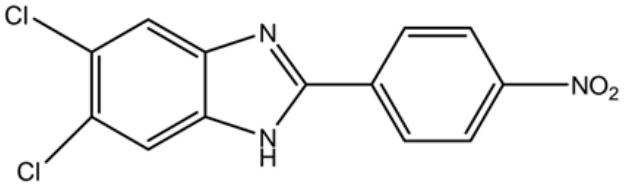
2) Imidazole as anti-inflammatory and analgesic activity: - *Kavitha C.S. et al*. synthesized a series of 2-methylaminibenzimidazole derivatives, and the newly synthesized compounds were tested for their anti-inflammatory and analgesic properties. This compound exhibits analgesic properties and is comparable to the common medication nimesulide.[17]



N-((6-bromo-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-chlorobenzenamine

Fig. 6

3) Imidazole as antiviral activity: - *Michele Tonelli et al* synthesized seventy-six 2-phenylbenzimidazole derivatives and evaluated for cytotoxicity and anti-viral activity against a panel of RNA and DNA viruses. Compound ([5,6-Dichloro-2-(4-nitrophenyl) benzimidazole]) exhibited a high activity resulting more potent than Reference drugs smycophenolic acid and 6-azauridine.[18]



5,6-dichloro-2-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole

Fig. 7

Pyrazole: -The term pyrazole was coined by Knorr in 1883. A class of simple aromatic heterocyclic chemicals known as pyrazoles gives humans pharmacological effects. Despite their rarity in nature, they are categorised as alkaloids. 1-pyrazolyl-alanine, the first naturally occurring pyrazole, was extracted from watermelon seeds in 1959. A common structural motif in many compounds with pharmacological activity is the pyrazole ring. This is mostly because of its adaptable pharmacological action and simplicity of production.[19]

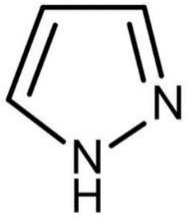


Fig. 8: Pyrazole.

In pyrazole, a five-membered ring heterocycle, the N-atom at position 1 is acidic because it is an imide, and pyrazole can readily lose this proton in the presence of a base. In contrast, the N-atom at position 2, which has two electrons, is basic and reacts with electrophiles. Because of their planar conjugated ring structure with six delocalised π-electrons, pyrazoles are aromatic in nature.[20]

For pyrazole, various tautomeric structures can be written. Three tautomeric forms of unsubstituted pyrazole are possible.

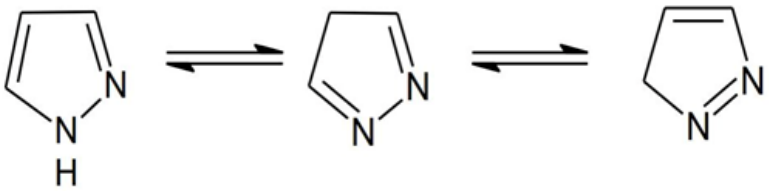
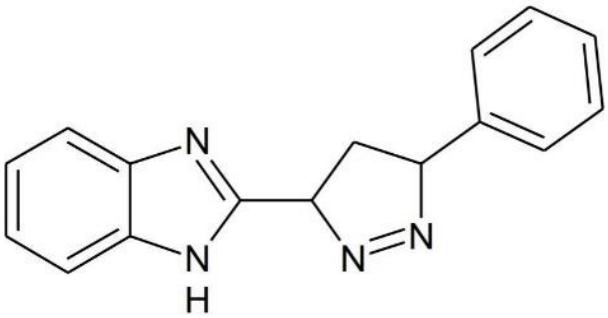


Fig. 9

Many compounds containing pyrazole nuclei have been shown to exhibit a wide range of biological action in recent years, including antibacterial, antiviral, insecticides, fungicides, anticancer, antihistaminic, and antidepressants. The pyrazole ring is an important synthetic pathway in the pharmaceutical industry because of its broad variety of biological activity. The fundamental structure of many medications is represented by such a heterocyclic moiety.[21]

- **Structures and it's pharmacological activity**

1) Pyrazole as anticancer agents: - *R. Kalirajan* et al synthesized a series of pyrazole Derivatives and these derivatives show anticancer activity.[22]



2-(1H-benzimidazol-2-yl)-4-phenyl-1,3-thiazole.
Fig. 10

2) Pyrazole as anticonvulsant activity: - Additionally, *Anoop Singh and colleagues* synthesised a number of 1-[(4, 5-dihydro-5 phenyl-3 phenyl amino) pyrazole-1 yl] ethanone derivatives and assessed their anticonvulsant properties. Rejecting the convulsion technique caused by electric shock.[23]

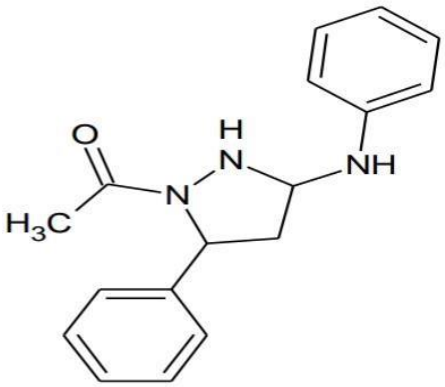


Fig. 11

Triazole: -The class of heterocyclic compounds known as triazoles 1 has been the subject of research for a long time. Triazoles are a pair of isomeric chemical compounds with the molecular formula C2H3N3 that consist of two carbon atoms and three nitrogen atoms arranged in a five-membered ring. Through a range of non-covalent interactions, azole rings can easily engage with a number of enzymes and receptors in biological systems, exhibiting a wide range of biological functions. The chemistry of triazoles and their fused heterocyclic derivatives has drawn a lot of attention lately because of its practical biological significance and synthetic value.[24]

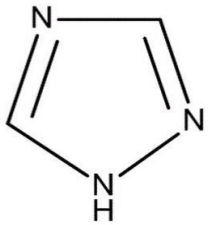
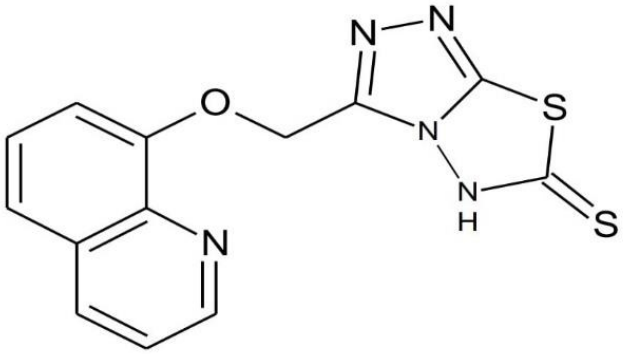


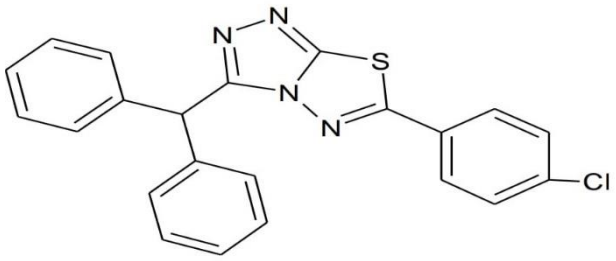
Fig. 12: Triazole.

- **Structures and it's pharmacological activity**
- **1) Triazole as antimicrobial activity: -**Mohamed S. B. et al. synthesised a number of triazole derivatives and evaluated their antifungal and antibacterial properties. Amphotericin B and tetracycline were the usual medications.[25]



3-{[(quinolin-8-yl) oxy] methyl} [1,2,4] triazolo[3,4-b] [1,3,4] thiadiazole-6(5H)- thione
Fig. 13

2) Triazole as anti-inflammatory agent: - Mohd. Amir et al synthesized 3-diphenylmethyl-6-substituted-1,2,4-triazolo[3,4-b]-1,3,4 thiadiazoles: A condensed bridgehead nitrogen heterocyclic system and evaluated for Anti-inflammatory activity by the carrageenan induced paw oedema test in Wistar albino rats by Winter et al. (1962) method. The standard drug was ibuprofen.[26]



6-(4-chlorophenyl)-3-(diphenyl l methyl) [1,2,4] triazolo [3,4-b] [1,3,4] thiadiazol
Fig. 14

CONCLUSION

Five-membered nitrogenated heterocyclic compounds represent a diverse and pharmacologically significant class of molecules. This review has highlighted the broad spectrum of pharmaceutical activities exhibited by these compounds, ranging from mention 2-3 specific examples of activities, e.g., antimicrobial, anti-inflammatory, and anticancer properties. The structural diversity within this class allows for significant modulation of biological activity, offering opportunities for the design and development of novel therapeutic agents. Further research focusing on mention a specific area for future research, e.g., structure-activity relationship studies and the exploration of novel synthetic pathways is warranted to fully exploit the therapeutic potential of these versatile heterocycles. Ultimately, the continued investigation of five-membered nitrogenated heterocycles promises to yield valuable new drugs for a wide range of diseases.

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