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# REVIEW OF TRIAZOLE DERIVATIVES: ITS SIGNIFICANT PHARMACOLOGICAL ACTIVITIES

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## ABSTRACT

Triazoles, a class of heterocyclic compounds containing a five-membered ring with three nitrogen atoms, have garnered significant attention in the field of organic and medicinal chemistry. This abstract provides an overview of the synthesis methods, structural diversity, and diverse applications of triazoles.

The synthesis of triazoles encompasses several approaches, including click chemistry, Huisgen cyclo addition, and transition metal-catalyzed reactions. These methods allow for the creation of a wide range of triazole derivatives with varying substituents and functional groups.

**Keywords:** Triazole , Antifungal Activity , antiviral activity , anticancer activity , antibacterial activity , anti-tubercular activity.

## 1. INTRODUCTION

Triazole is a five-membered ring compound containing two carbon atoms and three nitrogen atoms. It's an essential class of heterocyclic compounds with various applications in chemistry, agriculture, and medicine. In a professional context, you might encounter triazoles in fields like:

1. Chemistry: Triazoles serve as versatile building blocks in organic synthesis, often used in the creation of pharmaceuticals, agrochemicals, and advanced materials.

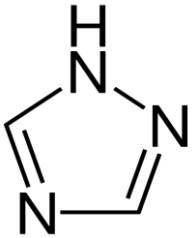
2. AGRICULTURE: Triazole fungicides are widely employed to protect crops from fungal diseases. They inhibit fungal growth by interfering with the biosynthesis of ergosterol, a vital component of fungal cell membranes.

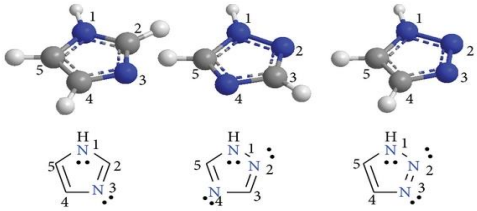
3. PHARMACEUTICALS: Triazole compounds are found in many pharmaceutical drugs, including antifungal medications (e.g., fluconazole) and antiviral drugs (e.g., ribavirin). They can also act as ligands in coordination chemistry for drug design.

4. COORDINATION CHEMISTRY: Triazoles are commonly used as ligands in coordination complexes due to their strong coordinating abilities. This has applications in catalysis and materials science.

In a professional setting, understanding the properties and applications of triazoles can be essential, depending on your specific field of expertise.

STRUCTURAL CHARACTERISTICS:





Triazole is a heterocyclic organic compound with a five-membered ring structure containing three nitrogen atoms and two carbon atoms. Its chemical structure is formally described as C2H3N3. The three nitrogen atoms and two carbon atoms in the triazole ring are arranged in a specific pattern, which imparts distinct structural characteristics:

1. Ring Structure: Triazole consists of a planar, five-membered ring. The ring is flat due to the sp2 hybridization of the nitrogen and carbon atoms, resulting in trigonal planar geometry at each atom in the ring.

2. Nitrogen Atoms: Three nitrogen atoms are part of the triazole ring. These nitrogens are adjacent to each other, forming a continuous chain of nitrogen atoms within the ring.

3. Carbon Atoms: Two carbon atoms are present in the triazole ring, interspersed among the nitrogen atoms. These carbons are also part of the ring structure.

4. Double Bonds: The triazole ring contains two carbon-nitrogen double bonds (C=N) and one carbon-carbon single bond (C-C). These double bonds contribute to the aromaticity of the ring.

5. Aromaticity: Due to the presence of alternating single and double bonds in the ring, triazole exhibits aromatic properties. It follows Hückel's rule for aromaticity, with 6π electrons in the ring, making it stable.

6. Functional Groups: Triazoles can have various functional groups attached to the ring, such as alkyl, aryl, or other substituents, which can modify their chemical properties and reactivity.

7. Isomerism: Triazoles can exist in several isomeric forms, including 1,2,3-triazole and 1,2,4-triazole, depending on the positions of the nitrogen atoms within the ring. [1-2]

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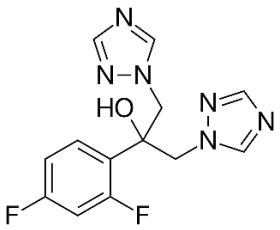
These structural characteristics make triazole a versatile and important class of compounds in organic chemistry, with a wide range of applications in pharmaceuticals, agriculture, materials science, and more. Understanding the detailed structure of triazoles is crucial for their synthesis and manipulation in various chemical processes.

**PHYSICAL PROPERTIES :**

| Properties | |
|---|---|
| Chemical formula | C2H3N3 |
| Molar mass | 69.00725 |
| Appearance | white solid |
| Density | 1.439 g/cm3 |
| Melting point | 120 to 121 °C (248 to 250 °F; 393 to 394 K) |
| Boiling point | 260 °C (500 °F; 533 K) |
| Solubility in water | very soluble |
| Acidity (pKa) | 10,3 |
| Basicity (pKb) | 11,8 |

The biological activity of triazole compounds is of significant scientific interest due to their diverse applications in pharmacology, particularly as antifungal and antiviral agents. Here's an overview of the biological activity of triazoles in a scientific manner:

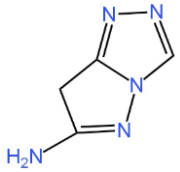
**Antifungal Activity:-**



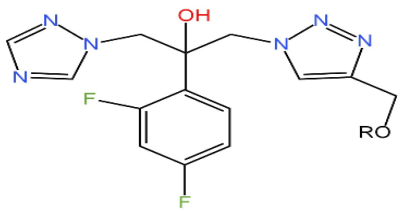

Triazoles are widely recognized for their potent antifungal properties.

Recently, there has been a development in number of antifungal drugs are available. Major five classes of antifungal compounds are currently in clinical use: allylamines, thiocarbamates, polyenes, fluoropyrimidines and azole derivatives. [3-6]

- They inhibit fungal growth by targeting the enzyme cytochrome P450 14α-demethylase (CYP51), involved in ergosterol biosynthesis, a critical component of fungal cell membranes.
- Prominent antifungal triazoles include fluconazole, itraconazole, and voriconazole, used to treat various fungal infections.
- M. M. Ghorab et al "synthesized some compounds were screened for their antifungal activity against species of fungi, P enicilium chrysogenum Thom (AUCC-530), Cundidu ulhicuns (Robim) Berkho (AUCC-1720 , Aspergillus ochruceus Wilhelm (AUCC-230) Aspergillus flavus Link (AUCC- 164) and), with new miscellaneous s-triazole and evaluated Ref: M. Ghorab et al synthesized and antifungal activity with new miscellaneous s-triazoles.




- Nilkanth G. Aher et al synthesized 1,2,3- triazole and evaluated antifungal activity by Cryptococcus neoformans and Candida albicans due to its potent activity by inhibiting cytochrome P51 by containing fluconazole analogues.
  Ref : Nilkanth G. Aher et al "synthesized antifungal activity by using analogues of fluconazole" Bioorganic & Medicinal Chemistry Letters 19 (2009) 759–763



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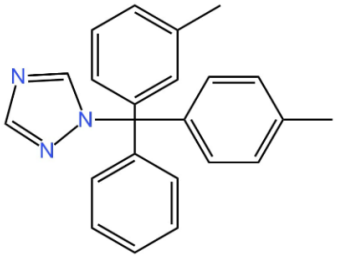
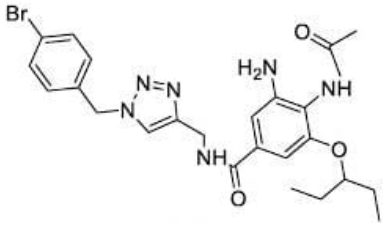
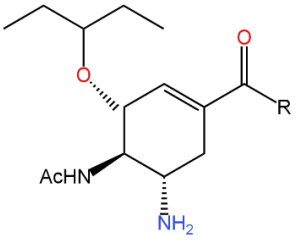
- Zahra Rezaei et al synthesized triazole and benzotriazole derivatives and evaluated for invitro antifungal activity against fungi including E. floccosum, T. rubrum , M. canis and C. albicans T. mentagrophytes by inhibiting cytochrome P450 14a-demethylase using standard fluconazole and clotrimazole. Ref: Rezaei a et al "Design, synthesis, and antifungal activity of triazole and benzotriazole derivatives" European Journal of Medicinal Chemistry 44 (2009) 3064–3067



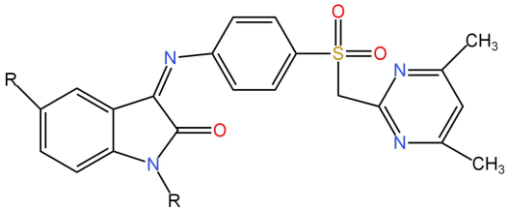
**Antiviral Activity:**



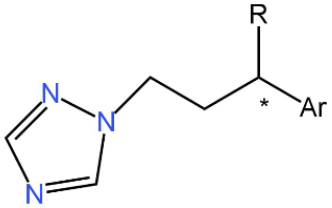
- Some triazole derivatives exhibit antiviral activity against a range of viruses, including HIV and hepatitis C virus (HCV). It affects a large part of population, as shown in a recent epidemiological study in Latin America and the Caribbean that estimated about 90% of adults and 60% of children are infected by HSV-1 [7].
- 5N1, H5N2, H5N6 in both enzymatic assay and cellular assay [8] Han Ju et al. reported a new class of 1,2,3-triazole oseltamivir analogues and screened their antiviral activity against three different strains (H
  European Journal of Medicinal Chemistry 139:718–725



- HIV is a virus that weakens the immune system in humans over time, making them susceptible to various infections. M asif tested different compound such as 4-[(1,2-dihydro-2-oxo-3Hindol-3-ylidene)amino]-N(4,6-dimethyl-2- pyrimidinyl)-benzenesulphonamide and its derivatives to see if they can help fight against HIV and found active against replication of HIV-1 and HIV-2 in MT-4 cells.
- Ref M asif "synthesized activities of Triazole analogues as antibacterial, antifungal, antiviral agents".



- Xiufang Cao et al synthesized novel triazole derivatives and evaluated for invitro antiviral activity against the CVB3 and EV71 in the corresponding HEp-2 and RD cells were evaluated that thirteen synthetic triazole derivatives inhibited RD cells by the CPE of EV71.
- Ref; Xiufang Cao et al "synthesized novel triazole derivatives and their in vitro antiviral activity". Wang, W., Cao, X, , Wang, S., & Bao, L. (2017). Asymmetric synthesis of novel triazole derivatives and their in vitro antiviral activity and thier mechanism of action. From European Journal of Medicinal Chemistry 139, 718–725.



- They can inhibit viral replication by interfering with viral enzymes or other essential processes.

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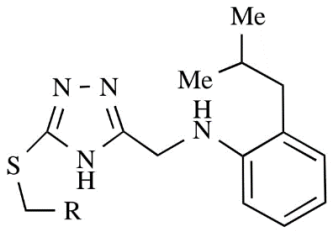
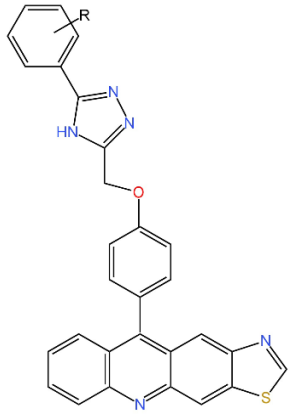
**Anticancer Activity:**

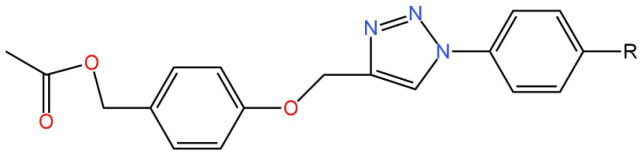


- Scientists are putting a lot of effort into developing improved medications for cancer. Some of these new drugs, such as anastrozole, letrozole, and vorozole, belong to a group known as triazole compounds. These drugs are crucial for treating cancer, particularly breast cancer.
  Certain triazole-containing compounds have shown promise as potential anticancer agents.
- They may act by inhibiting specific enzymes or signaling pathways involved in cancer cell proliferation and survival.[9]
- Mahanti et al. Evaluated and reported a series of fused acridine containing 1,2,4-triazole derivatives. And screened their anti-proliferative activity towards several human cell lines including, A375 (Melanoma), HT-29 (Colon), A549(Lung), MCF7 (Breast), and and Result revealed that the compounds exhibited the better anticancer activity. SAR investigations of this series revealed that introduction of 4-chloro, 3,4,5-(CH3O)3, and 4- CF3CH3 groups at para-position of the phenylring displayed the significant anticancer activity[10]

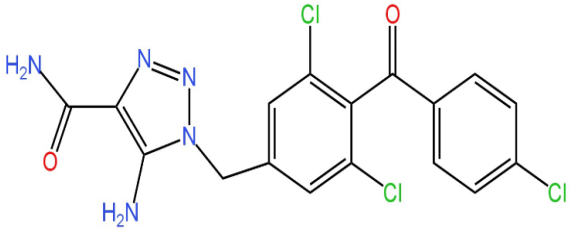


- Irfan Sahin et al synthesized the above given compounds were screened for cytotoxic activity against Hela cell line. Hela cells were treated with increase in concentrations of given compound for 48 hours and MTT cell proliferation assay were carried out for determination of the antiproliferative effects of agent on these cells.

Ref : Irfan Sahin et al "synthesized Anticancer Activity of 1,4-Disubstituted 1,2,3-triazoles"

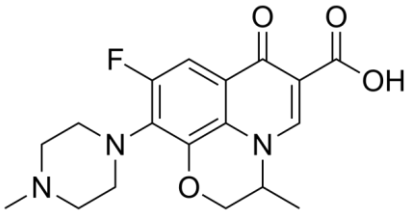


- Zhi Xu et al synthesized binaphthylamino tethered 1,2,3-triazole dimer IC50: 9.13 and 5.53, MTT assay) showed activity against A549 and HeLa cancer cell lines, and it was non-toxic towards normal mouse myoblast C2C12 cells.
  Ref; Zhi Xu et al "synthesized 1,2,3-Triazole-containing hybrids as potential anticancer agents"

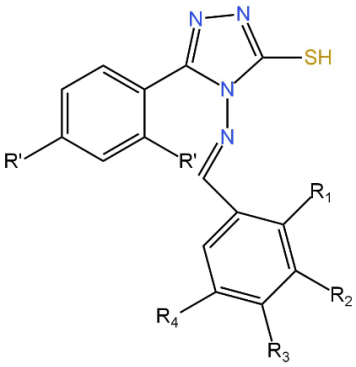


**Antibacterial Activity:**

- Tackling Drug-Resistant Infections Globally: Final Report and Recommendations", which was a result of an extensive work carried out by an independent commission, drug-resistant infections may be the cause of 10 million deaths annually by 2050, exceeding the number of deaths attributable to road traffic accidents and even cancer. [11]
- There are newly synthesized 1,2,4-triazole compounds were tested for their in vitro growth
- inhibitory activity against standard Gram-negative and Gram-positive bacterial strains.
- A large number of 1,2,4-triazole hybrids with (fluro)quinolone drugs have been incorporated into therapeutically interesting drug candidates in light of their potent antimicrobial effect, especially against resistant bacterial strains [12]
- They may target bacterial enzymes or processes critical for bacterial growth..

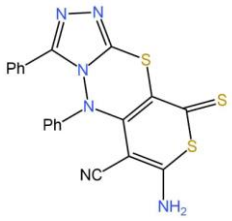


- Triazoles have been explored for their antibacterial properties, although they are primarily known for antifungal activity.
- Deepa Gupta et al synthesized 1,2,4-Triazole derivatives against bacterial strain S.aureus and E. coli and evaluated effective against the bacteria.
  Ref; Deepa Gupta et al "synthesized novel 1,2,4-Triazole derivatives for antifungal and antibacterial activity.

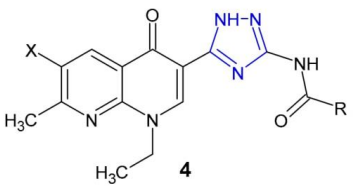


- Abd El-Badih A. G. Ghattas et al synthesized 1,2,3-Triazole-containing hybrids as potential anticancer agents in in vitro growth of broad spectrum of bacteria representing two species of Gram negative bacteria, namely Escherichia coli and Pseudomonas aeruginosa one species of Gram positive bacteria, name as Bacillus cereus by Some New S-Triazole Derivatives.

Ref; Abd El-Badih A. G. Ghattas et al "Synthesis and reported an Antibacterial Activity of Some New S-Triazole Derivatives"



- Novel nalidixic acidbased 1,2,4-triazole-3-thione derivatives 1–2 (Figure 4) were synthesized by Aggarwal et al. (2011) and screened against d screened against Gram-positive (S. aureus, B. subtilis) and Gram-negative bacteria (E. coli, K. pneumoniae, P. aeruginosa)[13]



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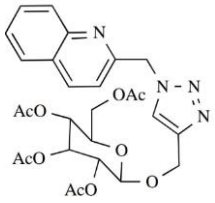
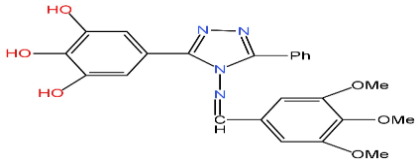
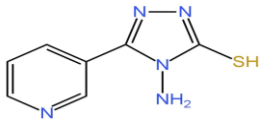
Anti-tubercular activity :



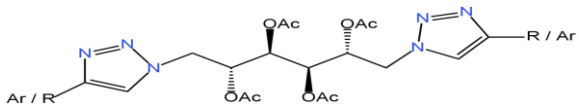
- 1,2,3-Triazole compounds have opened up new opportunities to create better drugs for treating tuberculosis. When scientists add a 1,2,3-triazole part to these drugs, it can make them more effective against tuberculosis.
- Sudeep K. Mandal et al Synthesized 3, 4, 5-trihydroxybenzohydrazide( Galloyl hydrazide ) in various ways in which one derivatives of substituted 1,2,4-triazol-3-yl)benzene-1,2,3-triol. To know their anti-tubercular activity.
  Ref; Sudeep K. Mandal et al "synthesized some triazole derivatives of propyl gallate for an Anti-tubercular activities"



- Farzana Afreen et al synthesized compound Pyridine potassium dithiocarbazate and Pyridine-4-carbohydrazide and screened against M. tuberculosis by using Microplate Almar Blue Assay (MABA). Ref; Farzana Afreen et al "synthesized a triazole derivative and evaluation of their antitubercular activity.



- Marcelle de L. Ferreira et al synthesized Five bis-1,2,3-triazole hybrids from D-mannitol and evaluated for their in vitro anti-TB activities against MTB H37Rv ATCC 27294 using the Alamar Blue susceptibility test. To determine anti-tubercular activity Ref; Marcelle de L. Ferreira 'synthesized Antitubercular Evaluation of New Bis-1,2,3-Triazoles Derived from D-Mannitol".



## 2. CONCLUSION

Triazoles exhibit diverse pharmacological activities, making them versatile compounds in medicinal chemistry. Their potent antifungal properties, notably seen in drugs like fluconazole and voriconazole, have been crucial in treating various fungal infections. Additionally, certain triazole derivatives demonstrate antiviral activity, inhibiting viral replication by interfering with essential processes. In the realm of cancer treatment, triazole-containing compounds, such as anastrozole and letrozole, show promise in inhibiting specific enzymes or signaling pathways involved in cancer cell proliferation. Triazoles have also been explored for antibacterial and anti-tubercular activities, providing new avenues for combating drug-resistant bacterial strains and tuberculosis. However, it is essential to monitor potential side effects and interactions, emphasizing the importance of careful clinical use and ongoing research in this field.

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