



A Review Article on Triazoles and its Pharmacological Activities

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Despite the fact that triazole was first synthesised over a century ago, it continues to unique the interest of chemists, biologists, technologists, and other experts. Triazoles have been shown to have antiviral, anti-inflammatory, anti-fertility, anti-tubercular, antimicrobial, anti-cancer, and anti-corrosion properties in recent years. The goal of this review is to describe the structures, synthesis, reactions, and spectral properties of triazoles in order to highlight their potential applications in a variety of bioactive phenomena and analytical applications.

Keywords: triazole ,synthesis and pharmacological activities

1. INTRODUCTION

Heterocyclic chemistry is a distinct branch of organic chemistry with a long history and

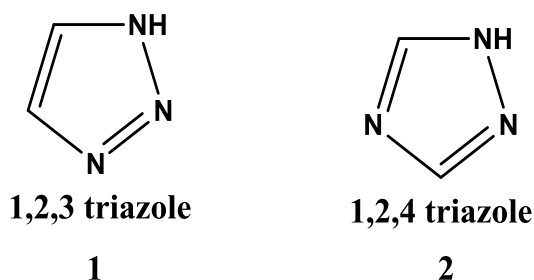
promising future. Heterocyclic compounds, such as purine and pyrimidine bases, are essential for life (building unit of DNA and RNA). Heterocyclic chemistry now contributes reagents and

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synthetic methods to the synthesis of drugs [1], pesticides [2], and detergents [3], as well as to related fields like biochemistry [4], polymers [5,6], dyes [7,8], and material sciences [9].

- **1,2,4-Triazole**

The triazole is a fascinating class of compounds defined by the presence of three nitrogen heteroatoms in five-membered ring systems. There are two types of triazoles: 1,2,3-triazoles (1) and 1,2,4-triazoles (2).



Five-membered nitrogen heterocycle compounds [10-15] are important structural fragments that are used as biologically active compounds, corrosion inhibitors [16], pesticides [17], dyes [18], acidbase indicators [19], and other industrial chemicals [20]. Bladin was the first scientist to name the carbon nitrogen ring system ($C_2N_3H_3$) and describe triazole derivatization in 1885.

2. TRIAZOLE STRUCTURAL PROPERTIES

- **Aromaticity and Stability**

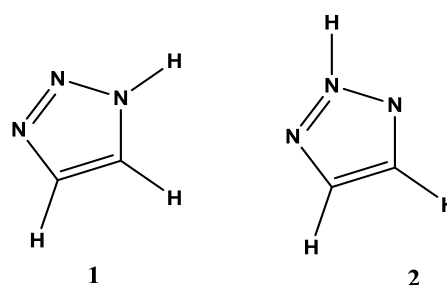
The main reason for the triazole nucleus stability is its aromaticity. The donation of one electron from each atom connected by double bonds, plus the remaining two electrons from a nitrogen atom, forms an aromatic sextet [21]. Furthermore, resonance stabilises the triazole nucleus, allowing it to be represented by tautomeric forms [22].

- **Tautomerism in Triazoles**

Tautomerism is possible in both the structural isomers of triazoles.

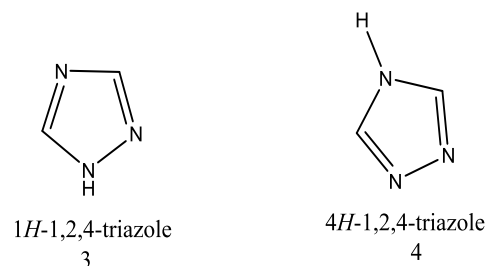
2.1 Tautomerism in 1,2,3-triazoles

1H-1,2,3-triazole (1) and 2H-1,2,3-triazole (2) are the two tautomeric forms of 1,2,3-triazoles [23].



2.2 Tautomerism in 1,2,4-triazoles

1, 2, 4-Triazoles have two tautomeric forms: 1H-1, 2, 4 triazole (3) and 4H-1,2,4-triazole (4) [24]. Many studies have shown that tautomer (3) is more stable than tautomer (4).



Barot and colleagues reported antibacterial and antifungal activities of a series of novel 1,2,4-triazole-5-thione derivatives of benzimidazole (5) with MICs of 2.0 and 2.5 g/ml; some of the synthesised compounds demonstrated good antibacterial and antifungal activity. Antibacterial activity was demonstrated against *Bacillus cereus*, *Enterococcus faecalis*, *Staph aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Candida albicans*, *Aspergillus niger*, and *Fusarium oxyspora*. Antibacterial activity against *Candida albicans*, *Aspergillus niger*, and *Fusarium oxyspora* was measured using Ofloxacin and Metronidazole, while antifungal activity was measured using Fluconazole [32].

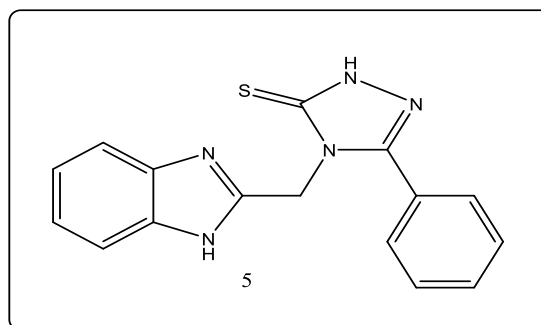
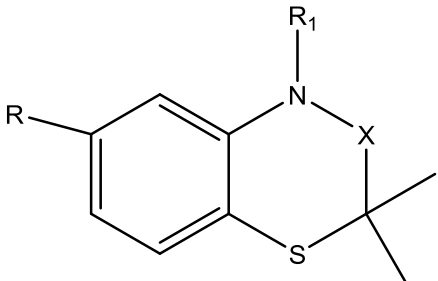
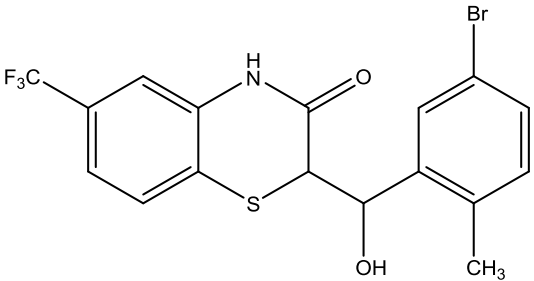
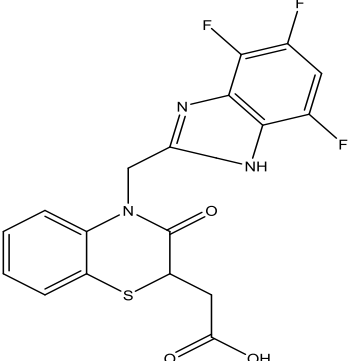
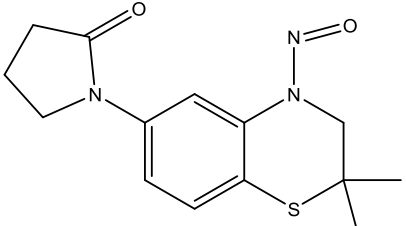


Fig. 1. Novel 1,2,4-triazole derivatives with morpholine moiety

Sahin and his coworkers synthesised Novel 1,2,4-triazole derivatives with morpholine moiety (6) and tested for antimicrobial activity. Tested microorganisms were *E. coli*, *E. aerogenes*, *Y. pseudotuberculosis*, *P. aeruginosa*, *S. aureus*, *E.*

faecalis, *B. cereus*, *M. smegmatis*, *C. albicans*, *C. tropicalis*, *Aspergillus.niger*, and *S.cerevisiae*. Ampicillin, streptomycin, and fluconazole were the standard antibiotics. [33]

Table 1. Pharmacological activities of Sulphur containing heterocycles

Sulphur Containing Heterocycles	Activity	Reference
 <p>R=H,CF₃, Br, NO₂, CF₃, CN R₁ = H,CH₂=CH₂, COCH₂Cl, CSNHCH₂Ph X= CO ,CH₂</p>	Vasorelaxant/ KATP- Channel Openers	25
	Vasorelaxant	26
	Antidiabetic	27
	KATP Channel Openers Vasorelaxant	28

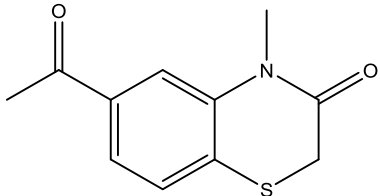
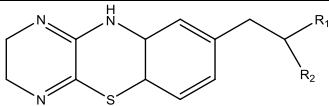
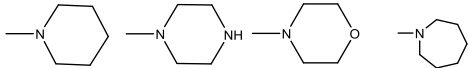
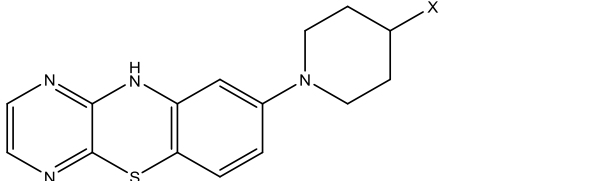
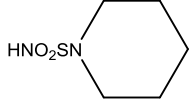
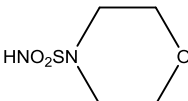
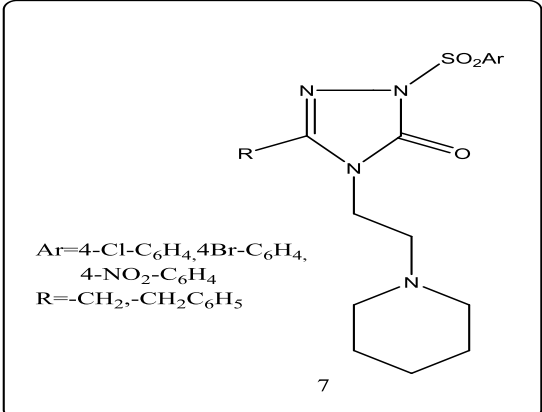
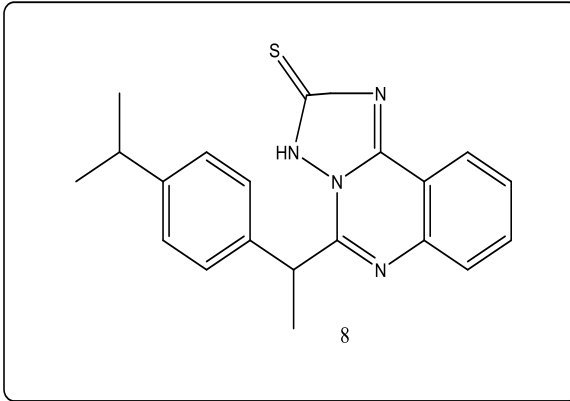
	Apoptosis	29
	Intercellular adhesion molecule-I (Icam-I)	30
NR ₁ R ₂ =		
		
	Intercellular adhesion molecule-I (Icam-I)	31
<p>X=NHCOMe, NHSO₂Me, CH₂NHSO₂Me, CH₂CH₂NHSO₂Me, NHSO₂Ph, NHSO₂NMe₂,</p>		
NHSO ₂ NH ₂		
		
 <p>Ar=4-Cl-C₆H₄, 4Br-C₆H₄, 4-NO₂-C₆H₄ R=-CH₂, -CH₂C₆H₅</p> <p>7</p>		
 <p>8</p>		

Fig. 2. Deravatives of Ibuprofen

Abdulla and his Coworkers synthesised deravatives of Ibuprofen(8) by cyclization under various reaction conditions they obtained promising results and they screened for microbial inhibitory effect by using new agents assessed in vitro against *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative) using cup-plate method. In that three compounds showed highest antibacterial activities compared to other compounds and standard drugs [34].

Fig. 3. 3-(3,4-substituted-phenyl)-4-(4-fluorophenyl)-5-methyl-4H-1,2,4-triazoles derivatives

Desabatinna and his colleagues synthesised derivatives of 3-(3,4-substituted-phenyl)-4-(4-fluorophenyl)-5-methyl-4H-1,2,4-triazoles (9) and tested them for antimicrobial activity. It was tested using Gram positive bacteria (*Staphylococcus aureus*, *Bacillus cereus*), *Escherichia coli* NCCS 265 and *Pseudomonas aeruginosa*, while antifungal activity was tested using *Aspergillus niger* and *Candida albicans*. To

improve the pharmacological properties of 1,2,4-triazoles, alkyl, alkoxy, and halogen substituents were used. The minimum inhibitory concentration was determined using the broth dilution method. Halogen substituted compounds were found to have superior antimicrobial properties [35].

Gupta and colleagues developed a series of 4-(4-substituted benzylideneamino)-2(morpholinomethyl)-5 (substitutedphenyl) -2H-1,2,4-triazole-4(4H)thione was synthesised by combining a Schiff base with formaldehyde and morpholine to produce an iminium ion. Antifungal screening revealed that five compounds are more effective against *Aspergillus niger* (MIC 64 g/mL) than fluconazole (the standard antifungal drug). Some synthesised compounds have the same antifungal activity as fluconazole, with a MIC of 32 g/mL. The presence of electronegative groups, 4-chloro, and 2,4-dichloro groups at the aryl moiety attached to the 5th position of the triazole nucleus is credited with the high activity [36].

B. Andrews and his Coworkers reported a series of pyrimidine-bearing 1,2,4-triazoles were synthesised and tested for antifungal activity. When compared to the standard drug Amphotericin-B, the majority of the compounds showed promising antifungal activity. *Candida albicans*, *Penicillium sp.*, and *Aspergillus niger* were used to test these compounds for antifungal activity. At a concentration of 10 g/ml, the majority of the synthesised compounds showed moderate to good inhibition. However, when compared to standard drugs, the activity was lower [37].

Sachdeva synthesised Spiro indole-triazoles, and they were tested for antibacterial activity against Gram-positive *Bacillus licheniformis*, *Staphylococcus aureus* and *Micrococcus luteus*, as well as Gram-negative bacteria *E. coli* and *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* and *Escherichia coli* are two bacteria that cause infections. Antifungal activity was tested against *Aspergillus niger*, *Penicillium sp. fusarium oxysporum*, *Alternaria brassicicola*, *Chaetomium orium*, and *Lycopodium sp.* at concentrations of 500 ppm and 250 ppm. Streptomycin and erythromycin were used as reference standards. At 500 ppm concentrations, one compound showed excellent activity against the bacteria *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Micrococcus luteus* [38].

Jin-Xia Mu Synthesised and screened for Herbicidal Activity of 1,2,4-Triazole as a Moiety of Pyrazole. The majority of the synthesised compounds had a moderate herbicidal effect on lettuce and bent grass. Compounds 11 had the strongest herbicidal activity against lettuce and bent grass (80% inhibitory) [38,39].

An improved blend of 1,3,5-trisubstituted 1,2,4-triazoles has been accounted for through 1,3-dipolar cycloaddition of nitrile imine, created in situ from 14 within the sight of Ag_2CO_3 and Et_3N . In an elective two-venture approach, Buzykin et al originally pre-arranged halfway from the response of with an essential amine and Et_3N , which was then treated with an answer of 30% H_2O_2 /fluid KOH to yield. [40,41].

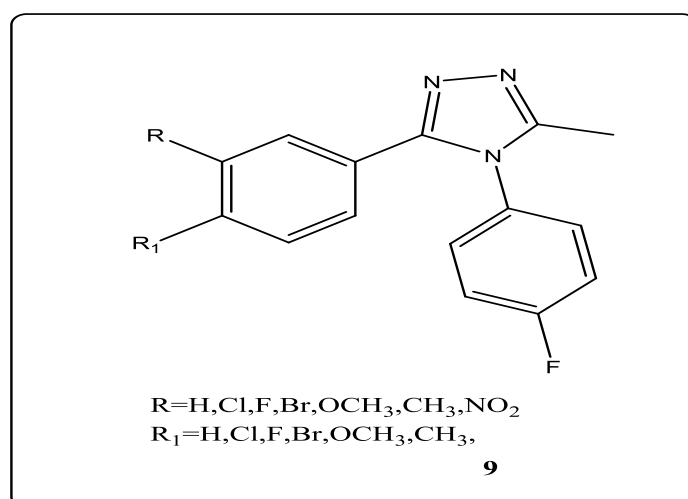


Fig .4. series of 4-(4- substituted benzylideneamino)-2(morpholinomethyl)-5(substitutedphenyl)-2H-1,2,4-triazole-4(4H)thione

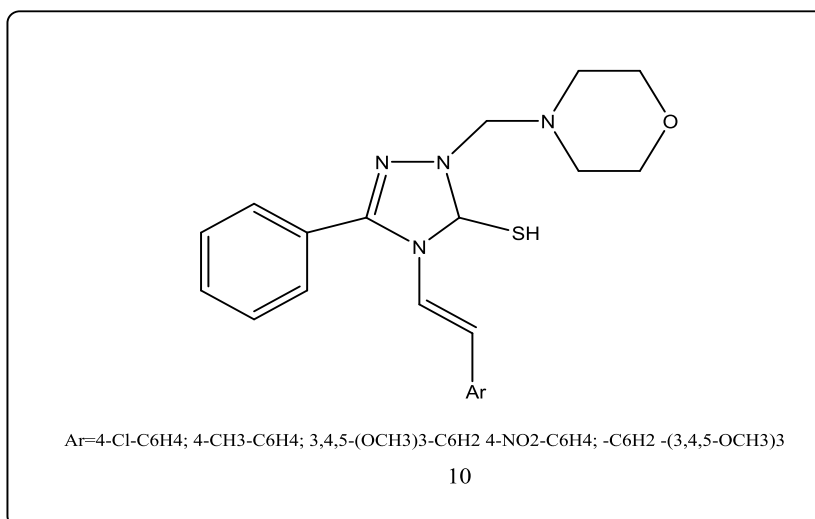


Fig. 5. Series of pyrimidine-bearing 1,2,4-triazoles

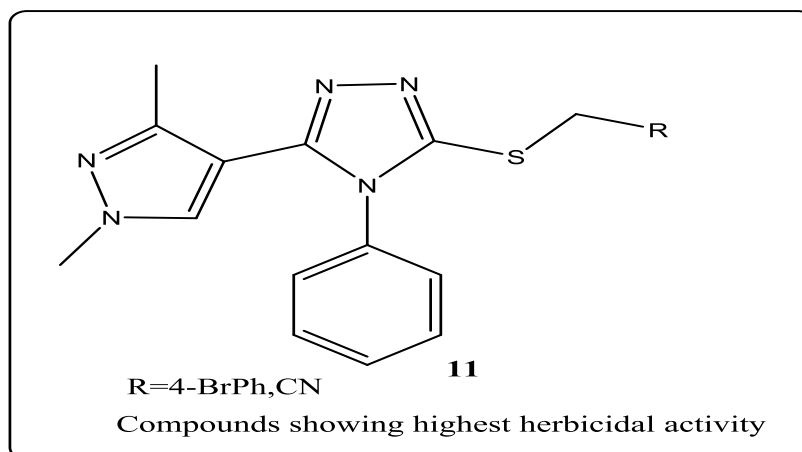


Fig. 6. Compound with high herbicidal activity

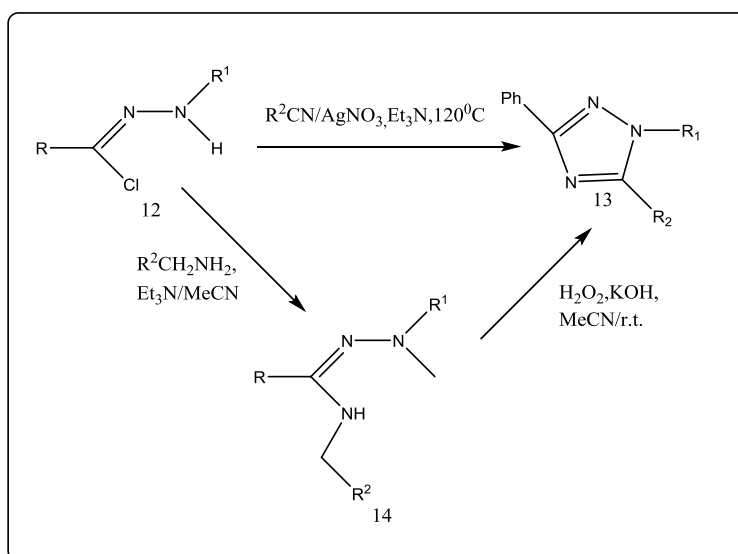


Fig. 7. Chemical transformation

3. CONCLUSION

As a result, this review covers the various synthetic routes used to produce a biologically rich triazole moiety, as well as the reactions that the molecule undergoes to produce other important molecules. It also emphasises the triazole rings therapeutic properties, as well as the wide range of drugs that contain the ring on the market. It also emphasises the therapeutic properties of the triazole ring, as well as the wide range of drugs on the market that contain the ring. As a result, this paper will benefit future research on the bioactive triazole ring.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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