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A REVIEW ON THE TRIAZOLES AND THEIR DERIVATIVES AS A POTENTIAL BIOLOGICAL ACTIVITY

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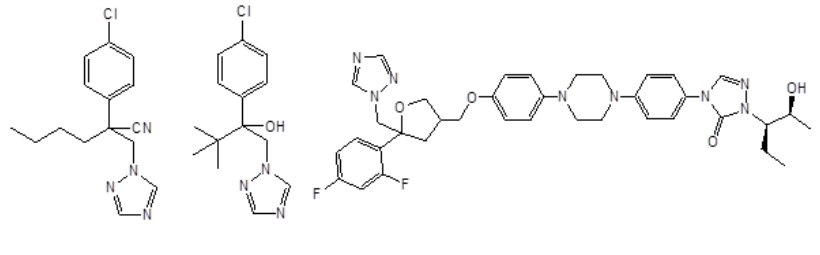
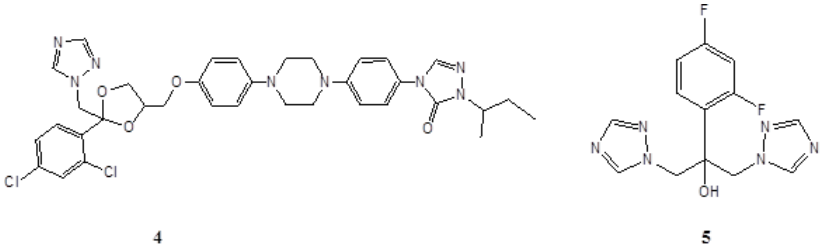
ABSTRACT
Significant biological activity such as anti-bacterial, anti-fungal, hypoglycemic activity, anti-inflammatory activity, antagonist activity and root elongation activity effects are possessed by both triazoles and their derivatives. Triazoles belong to the class of heterocyclic compounds. They exhibit a wide range of biological activities because their azole ring can easily engage with different enzymes and receptors in biological systems through a variety of non-covalent interactions.

KEYWORDS: Triazoles, Biological activity, Heterocyclic compounds, Azole.

INTRODUCTION

Triazoles are the class of heterocyclic compounds[1] their azole ring is readily able to bind with a variety of enzymes and receptors in biological system *via* diverse non-covalent interactions, and thus display versatile biological activities. Among the triazoles, 1,2,4-triazole have drawn great attention due to its wide variety of activities[2], many drugs which containing triazole moiety available in market such as antifungal drugs myclobutanil[3] (**1**), tebuconazole[4] (**2**), posaconazole[5] (**3**), Itraconazole[6] (**4**), fluconazole[7] (**5**) and paclobutrazole[8] (**6**), anticancer drugs anastrazole[9] (**7**), litrozole[10] (**8**) and vorozole[11] (**9**), antimigrain drug rizatriptan[12] (**10**) and antiviral drug ribavirin[13] (**11**). Further the detailed activities of triazoles are discussed in the following section.**Figure 1.**





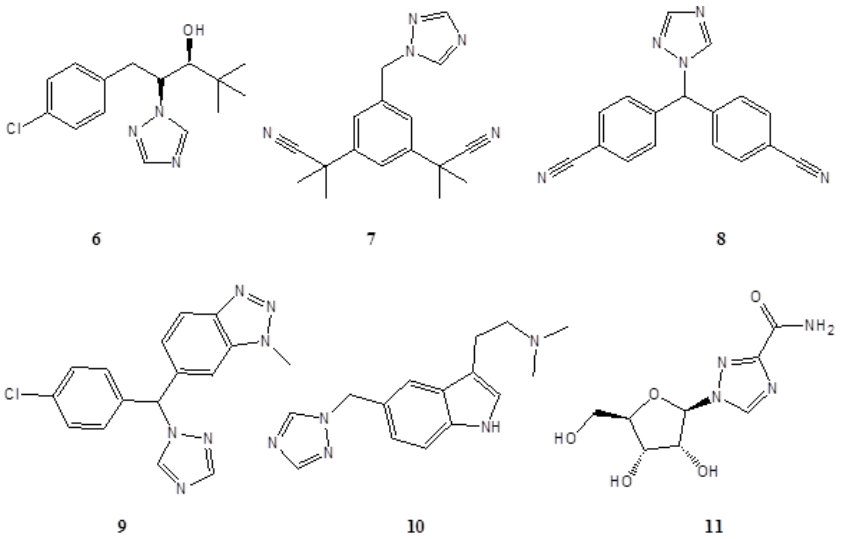


Figure 1

BIOLOGICAL ACTIVITY

Both triazoles and their derivatives have significant biological activity, including antibacterial, antifungal, hypoglycemic, anti-inflammatory, antagonistic, and root elongation properties. **Figure A**

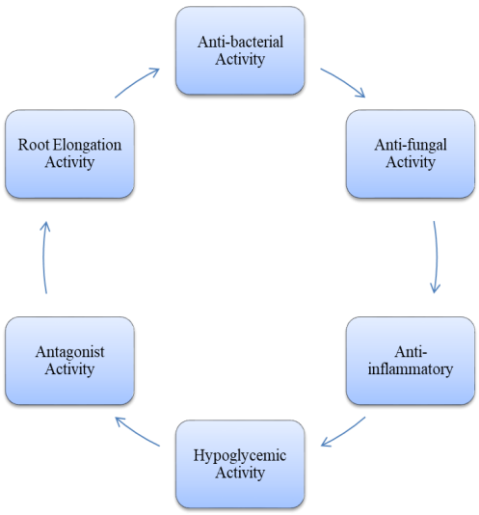
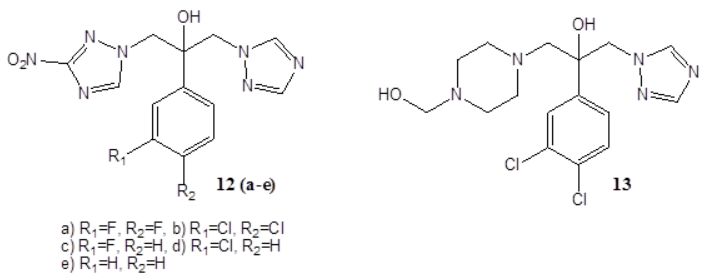


Figure A

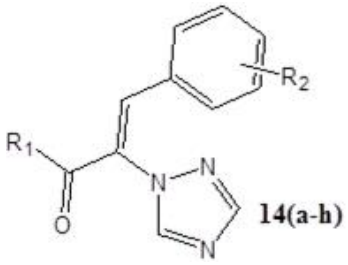
Figure 2: According to Sadeghpour *et al.*[14], using the Autodock 4.2 programme, a variety of fluconazole derivatives containing nitrotriazole (series A) or piperazine ethanol (series B) side chains were synthesised and docked in the active site of lanosterol 14-demethylase enzyme (1EA1). Then, utilising a broth microdilution assay against several standard and clinical fungi, the synthesised compound's antifungal properties were evaluated against a variety of natural and clinical strains of fungi. Against the majority of the investigated fungi, nitrotriazole compounds exhibited outstanding and desired antifungal activity. The nitrotriazole-containing compounds **12(a-d)** and **13** among the produced compounds displayed the strongest antifungal efficacy, particularly against a number of fluconazole-resistant organism.



a) R_1=F, R_2=F, b) R_1=Cl, R_2=Cl
c) R_1=F, R_2=H, d) R_1=Cl, R_2=H
e) R_1=H, R_2=H

Figure 2

Figure 3: Due to its vast range of biological activities, particularly its 1,2,4-triazole derivatives predominant antifungal activity, 1,2,4-triazole is a crucial scaffold in medicinal chemistry. Inhibiting the 14-alpha-demethylase enzyme is the latter's primary antifungal action mechanism (CYP51). Stingaci *et al*.[15] reprted the synthesis of triazole derivaties and evaluation of *in vivo* antibacterial activity and found that the MIC and MBC values ranging from 0.0002 to 0.0069 mM, all investigated drugs demonstrated strong antibacterial activity. Compound **14h**, followed by compounds **14f** and **14g**, seemed to be the most active of all those examined, with MIC values of 0.0002-0.0033 mM and MBC values of 0.0004-0.0033 mM. *Xanthomonas campestris* appeared to be the most susceptible bacterium, whilst *Erwinia amylovora* was the most resilient. The evaluation of antifungal activity revealed that compound **14h** displayed best antifungal activity with MIC at 0.02-0.04 mM and MFC at 0.03-0.06 mM.



a) R_1=Ph, R_2=3-OH,
b) R_1=4-Ph, R_2=4-$(CH_3)_2$
c) R_1=4-Cl-Ph, R_2=2-OH-5-NO_2
d) R_1=2-naphthyl, R_2=4-$(CH_3)_2$
e) R_1=2,4-di-Cl-Ph, R_2=H
f) R_1=2,4-di-Cl-Ph, R_2=4-NO_2
g) R_1=2,4-di-Cl-Ph, R_2=3,5-$(tBu)_2$-4-OH
h) R_1=Isobutyl, R_2=4-NO_2

Figure 3

Figure 4: According to Moise *et al*.[16], new 1,3,4-thiadiazole and 1,2,4-triazole derivatives with phenylalanine moiety were synthesised, and after testing them for toxicity and anti-inflammatory activity, it was found that compound **15** had anti-inflammatory activity that was comparable to other nonsteroidal anti-inflammatory drugs.

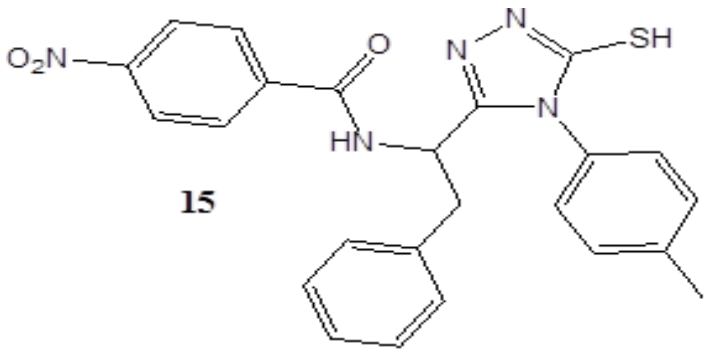


Figure 4

Figure 5: The synthesis of 3-[4-(4-substituted phenyl-5-thioxo-1*H*-1,2,4-triazol-3-ylmethoxy)-phenyl] was carried by Havaldar *et al*.[17] and evaluated their antibacterial activity. Compound **16** from the group that was examined had exceptional effectiveness against *Staphylococcus aureus* and *Bacillus subtilis*. Along with being effective against *A. niger* and *Cryptococcus neoformans*. The synthesised compounds were further evaluated for antimalarial activity, and only compound **16** was discovered to be most effective against strains of *Plasmodium falciparum*, with 50% inhibitor concentration (IC_{50}) values of 1.2 μM.

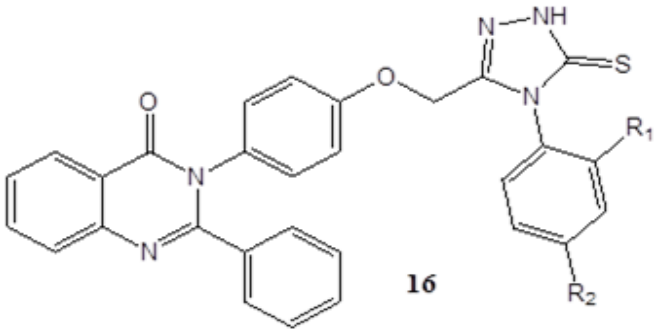


Figure 5

Figure 6: The 4-amino-5(2-aroylaryloxy)methyl-1,2,4-triazole-3(2*H*) thiones were synthesi- sed by Shaukath *et al*.[18] and tested against various bacterial and fungal strains. It was discovered that compound **17c** shown good activity in comparison to fluconazole and chloramphenicol, respectively.

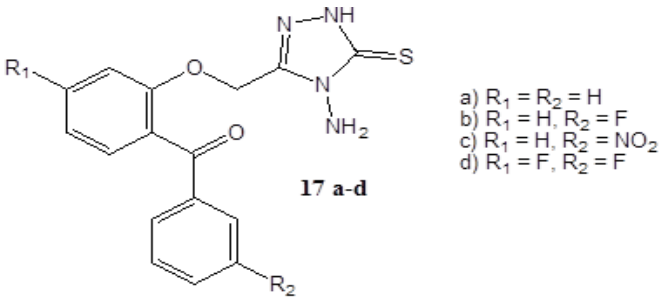


Figure 6

Figure 7: The synthesis of 4-alkyl-5-aryl-1*H*-1,2,4-triazole-3-thiol and testing of their hypoglycemic action in rats were both reported by Mhasalkar *et al*.[19] The most active compounds were 3-p-chlorophenyl-1-ethyl-4*H*-1,2,4-triazole-3-thiol **18** and 3-p-sulfamolylphenyl-1-ethyl-4*H*-1,2,4-triazole-3-thiol **19**, which both lowered blood sugar levels in rats and showed considerable activity in five different compounds. They exhibited no antibacterial effect and had a very low level of toxicit.

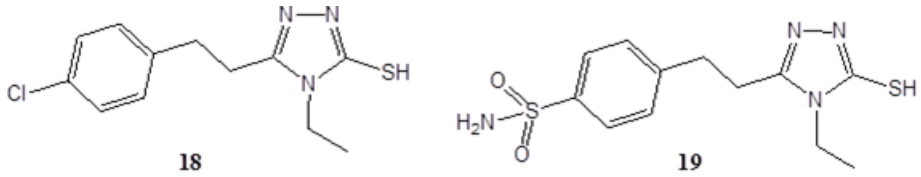


Figure 7

Figure 8: Novel 3-alkylthio-4-arylideneamino-5-(2-furyl)-1,2,4-triazole derivatives **20** were synthesised and evaluated for their endothelin receptor antagonist activity. A competitive binding experiment for the endothelin (ET) receptor revealed that some drugs were highly selective and effective ET-1 receptor antagonists. Endothelin (ET), a family of peptides released by endothelial cells, is crucial for the physiological process of vasoconstriction, and ET receptor antagonists are of great interest in the hunt for new treatments for the many cardiovascular disorders (CVDs).[20]

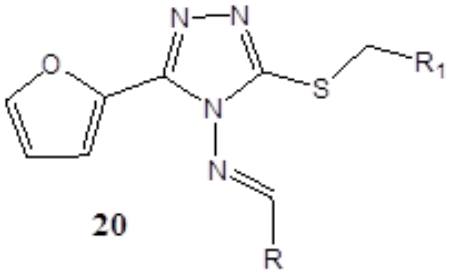


Figure 8

Figure 9: Numerous triazole derivatives were prepared and their oral hypoglycemic potential was tested. Each compound was tested using an oral single dose administration method in rats and/or dogs. The vast majority of the derivatives showed some level of activity. In both rats and dogs, 5-cyclohexyl-2-(p-tolurnesulfonamido)-1,3,4-triazole **21** was fairly effective, and upon daily dosing in dogs, hypoglycemia was maintained.[21]

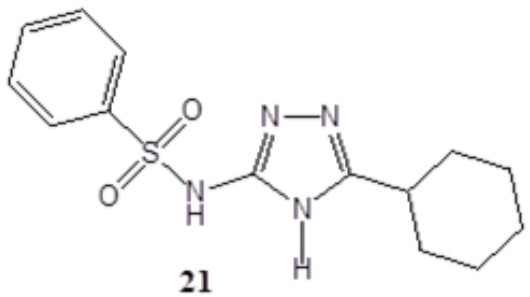
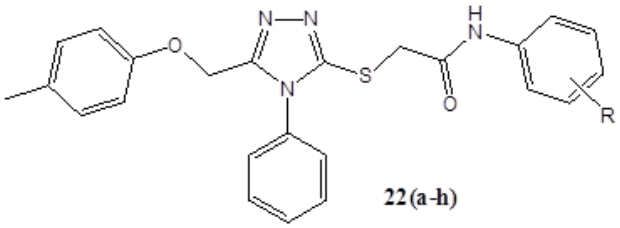


Figure 9

Figure 10: Triazole derivatives **22(a-h)** were synthesised by Wei *et al*.[22], and their potential to control plant growth was investigated. These compounds have been demonstrated to significantly improve root elongation. At high concentrations of 200 ppm, the majority of the compounds show inhibition action; yet, at low concentrations of 10 ppm, they show activity that enhances root elongation. It is noted that different functional groups introduced into the aniline ring at various positions result in an enhancement of the root elongation activity when compared to **22a**. p-substitution, followed by m- and then o-substitution, increases root elongation activity.



22(a-h)

R = a) H, b) 4-Cl, c) 3-Cl, d) 2-Cl, e) 4-CH_3, f) 3-CH_3, g) 2-CH_3, h) 4-OCH_3

Figure 10

CONCLUSION

This review outlined the triazoles and their derivatives served as a resource for both basic and applied research on the subject.

CONFLICTS OF INTEREST

There are no conflicts to declare.

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REFERENCES

1. Dixit, D.; Verma, P. K.; Marwaha, R. K. "A review on triazoles: their chemistry, synthesis and pharmacological potentials" J. Iranian Chem. Soc., 2021; 18: 2535-2565.
2. Jewad, S.; Yusra, A. "Chemistry of 1,2,4-triazole: A review article" Int. J. Sci. Res., 2016; 5: 1411.
3. Rodriguez, F. S.; Jimenez, A. L. O.; "Myclobutanil" Editor(s): Philip, W. Encyclopedia of Toxicology (Third Edition), Academic Press, 2014; 420-423.
4. De Albuquerque, N. C. P.; Daniel, B. C.; Habenschus, M. D.; de Oliveira, A. R.M. "Metabolism studies of chiral pesticides: A critical review" J. Pharm. Biomed. Anal, 2018; 147: 89-109.
5. Leaver, D. J. "Synthesis and biological activity of sterol 14-α-demethylase and sterol C24-methyltransferase inhibitors" Molecules, 2018; 23: 1753.
6. Zuckerman, J. M.; Tunkel, A. R. "Itraconazole: a new triazole antifungal agent" Infect. Control Hosp. Epidemiol, 1994; 15: 397-410.
7. Szeto, J.; Vu, V. A.; Malerich, J. P. "Multi-step continuous flow synthesis of fluconazole" J. Flow Chem., 2019: 35-42.
8. Soumya, P. R.; Kumar, P.; Pal, M. "Paclobutrazol: a novel plant growth regulator and multi-stress ameliorant" Ind. J. Plant Physiol., 2017; 22: 267-278.
9. Goss, P. E.; Tye, L. M. "Anastrozole: a new selective nonsteroidal aromatase inhibitor" Oncology, 1997; 11: 1697-703.
10. Sandhya Rani, M.; Srinivasa, L. "synthesis and characterization of letrozoleloaded polymer based nanoparticulate formulations" Neuroquantology, 2022; 20: 1077-1087.
11. Goss, P.E. "Pre-clinical and clinical review of vorozole, a new third generation aromatase inhibitor" Breast Cancer Res. Treat, 1998; 49(suppl 1): S59-S65.
12. Millson, D. S.; Tepper, S. J.; Rapoport, A. M. "Migraine pharmacotherapy with oral triptans: a rational approach to clinical management" Expert Opin. Pharmacother, 2000; 1: 391-404.
13. Paeshuyse, J.; Dallmeier, K.; Neyts, J. "Ribavirin for the treatment of chronic hepatitis C virus infection: a review of the proposed mechanisms of action" Current opinion in virology, 2011: 1: 590-598.
14. Sadeghpour, H.; Khabnadideh, S.; Zomorodian, K.; Pakshir, K.; Hoseinpour, K.; Javid, N.; Faghih, M. E.; Rezaei, Z. "Design, synthesis, and biological activity of new triazole and nitro-triazole derivatives as antifungal agents" Molecules, 2017; 22: 1150.
15. Stingaci, E.; Zveaghinteva, M.; Pogrebnoi, S.; Lupascu, L.; Valica, V.; Uncu, L.; Smetanscaia, A.; Drumea, M.; Petrou, A.; Ciric, A.; Glamoclija, J.; Sokovic, M.; Kravtsov, V.; Geronikaki, A.; Macaev, F. "New vinyl-1,2,4-triazole deriva- tives as antimicrobial agents: synthesis, biological evaluation and molecular docking studies" Bioorg. Med. Chem. Lett., 2020; 30: 127368.
16. Moise, M.; Sunel, V.; Profire, L.; Popa, M.; Desbrieres, J.; Peptu, C. "Synthesis and biological activity of some new 1,3,4-thiadiazole and 1,2,4-triazole compounds containing a phenylalanine moiety" Molecules, 2009; 14m: 2621-2631.
17. Havaldar, F. H.; Patil, A. R. "Syntheses of 1,2,4-triazole derivatives and their biological activity" E-Journal of Chem., 2008; 5: 347-354.
18. Shaukath, A. K.; Sheena, S. S.; Umesha, R. K. "Synthesis and antimicrobial study of novel heterocyclic compounds from hydroxybenzophenones" Eur. J. Med. Chem., 2005; 40: 1156-1162.
19. Mhasalkar, M. Y.; Shah, M. H.; Nikam, S. T.; Anantanarayanan, K. G.; Deliwala, C. V. "4-alkyl-5-aryl-4H-1,2,4-triazole-3-thiols as hypoglycemic agents" J. Med. Chem., 1970; 13: 672-674.
20. Liu, X. Y.; Xu, W. F.; Wu, J. "Synthesis of 4-amino-5-furyl-2-yl-4H-1, 2,4-triazole-3-thiol derivatives as a novel class of endothelin (ET) receptor antagonists" Chinese Chem. Lett., 2003; 14: 790-793.

21. O'Neal, J. B.; Rosen, H.; Russell, P. B.; Adams, A. C.; Blumenthal, A. “Potential hypoglycemic agents: 1,3,4-oxadiazoles and related compounds” J. Med. Pharm. Chem., 1962; 5: 617-626.
22. Wei, T. B.; Tang, J.; Liu, H.; Zhang, Y. M. “Synthesis and bioactivity of some new [3-[4-methylphenoxymethyl]-4-phenyl-[1,2,4]-triazole-5-thio]acetanilide derivatives” Indian J. Chem., 2007; 46B: 880-883.