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Recent advancement of triazole derivatives and their biological significance

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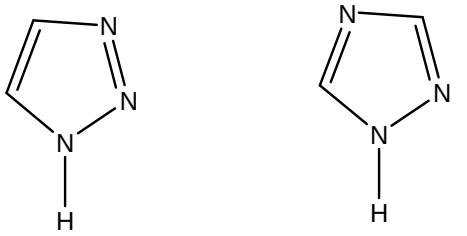
ABSTRACT

Article is based on the different pharmacological activity of the triazole ring, from a last decade a lot of work is going on, on the triazole ring , scientists develop a lot of new compounds related to this moiety and screened them for there different pharmacological activities to get a molecule which have good pharmacological activity and lesser side effect. This review article reflects various pharmacological activities of new triazole derivatives.This triazole has shown its importance as antimicrobial, anti-inflammatory, hypoglycemic, antidepressant, antitubercular, analgesic, anti-malarial and anticancer agents.

Keywords: Anti-microbial activity, Triazole, Anti-malarial, Antifungal, Anticancer.

INTRODUCTION

The chemistry of heterocyclic compound continuous to be an explore field in the organic or Pharmaceutical chemistry. The importance of triazole derivatives lies in the field that these have occupied a unique position in heterocyclic chemistry, due to its various biological activities.[1] Triazole refers to either one pair of isomeric chemical compound having membered ring of two carbon atom and three nitrogen atoms. The two isomers are **(fig:1)**



1,2,3 triazole 1,2,4 triazole

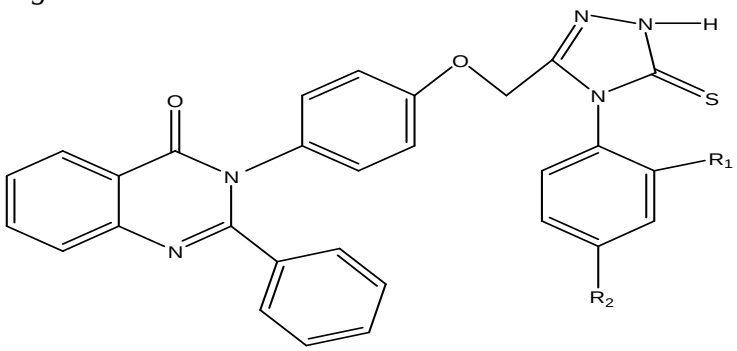
Fig: 1

The derivatization of Triazole ring is based on the phenomenon of bioisosterism in which replacement of oxygen of oxadiazole nucleus with nitrogen triazole analogue. Out of the two triazoles 1, 2, 4- triazole has wide variety of activity.[2] Triazole moiety is an important and frequent insecticide, agrochemical structure feature of many biological active compound as cytocrome p450 enzyme inhibitors and peptide analog inhibitor. The azole class of antifungal agent is chemical either an imidazole or a triazole group joined to an asymmetric carbon atom as their functional pharmacophore treatment for these infection azole like antifungal agent are Ketoconazole, Fluconazole , Voriconazole and Ptraconazole 1, 2, 4-triazole are as analgesic antiasthmatic, antibacterial, anticholinergic activity. They are aromatic ring compounds similar to the azole, pyrazole and imidazole but with an additional nitrogen atom in the ring structure. Like the azoles, triazoles are used in many antifungal drugs and fungicides, but the triazole-based drugs are more selective for fungi than mammalian cells than the azole-based antifungal compounds. [3]

BIOLOGICAL ACTIVITIES OF TRIAZOLE DERIVATIVES

Antifungal activity:

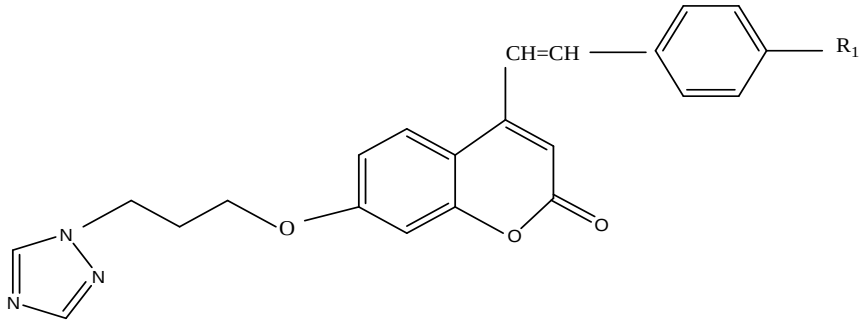
Freddy H. et al. synthesized a series of compound (2) 3-[4-(substituted phenyl-5-thioxo-4, 5-dihydro-1*H*-1,2,4 triazole-3-yl-methoxy)-phenyl]-2-phenyl-3*H*-quinazoline-4-one **(Fig:2)** screened for antifungal activity. The compound (2c) 3-{4-[-nitrophenyl)-5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazole-3-yl-methoxy]phenyl}-2-phenyl-3H-quinaolin-4-one exhibit good activity against *Aspergillus niger*. [4]



Compound	R_1	R_2
2a	H	H
2b	H	F
2c	H	NO_2

(Fig:2)

Ganesh R. Kokil et al. have synthesized a series of compound (3) 7-(3-(1H-1,2,3-triazole-1-yl)propoxy)-4methyl-2H-chromen-2-one **(Fig:3)** and screened for *in-vitro* antifungal activity against strain of *Candida albicans*. All compounds except compound (3a) showed moderate antifungal activity while compound (3c) 7-(2-(1H-1,2,3-triazole-1-yl)-4-(4-nitrostyryl)-2H-chromen-2-one which is nitro substituted at Para-position showed antifungal activity as comparable to Ketoconazole.[3]



Compound	R_1
3a	H
3c	NO_2

Fig: 3

Krzysztof Sztanke et al.synthesized series 3-(un)substituted-7-aryl-5H-6,7-dihydroimidazo[2,1-c][1,2,4]triazoles compounds and its derivatives which is **(Fig:4)** screened for antimicrobial and antifungal activities. 7-(4-Chlorophenyl)-5H-6,7-dihydroimidazo[2,1-c][1,2,4]triazole-3-thiol showed the superior antifungal activity as compared to Miconazole.[5]

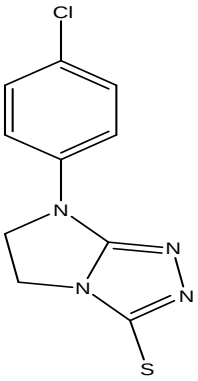


Fig: 4

Anti-bacterial activity:

Neeraj Upmanyu et al. have synthesized a series of 5-phenyl, 4-(substituted) amino, 3-mercapto 1, 2, 4-triazoles **(Fig:5)** which showed potent anti-bacterial activity.[2]

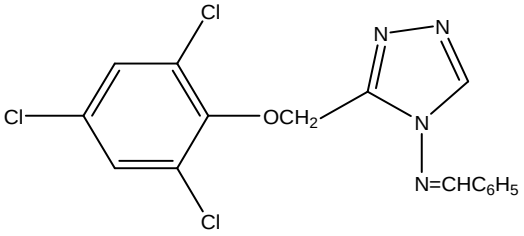


Fig:-5

A series 3-(un)substituted-7-aryl-5H-6,7-dihydroimidazo[2,1-c][1,2,4]triazole compound **(Fig:6)** are synthesized by **H.Singh et al**. Their anti-bacterial activity and its derivatives such as 3(2,4-Ddichlorophenoxymethyl)-7(3,4dichlorophenyl-5H-6,dihydroimidazo[2,1c][1,2,4]triazoles showed superior *in vitro* anti-bacterial activity then compared to Ampicillin and Chloroamphenicol.[6]

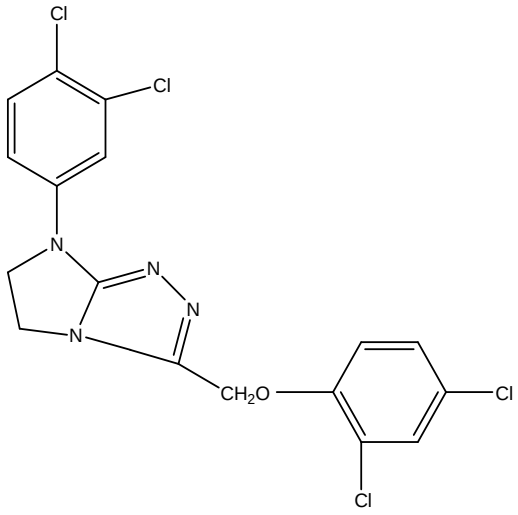
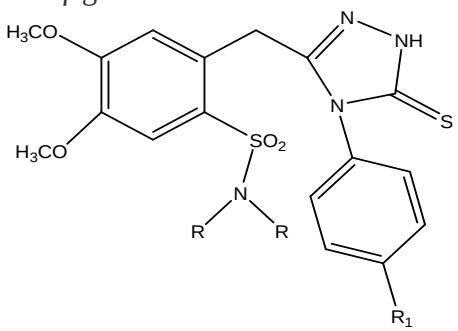


Fig: 6

Charalabos Camoutsis et al. synthesized a series of compound 5-[2-(substituted sulfamoyl)-4,5-dimethoxy-benzyl]-4aryl-s-triazole-3-thiones **(Fig:7)** and screened for anti-bacterial activity and its series derivative compound 7a,7b and 7c showed inhibitory effect at 100.0 µg/ml against *Escherichia coli*, which has the same MIC as antibiotic Streptomycin but much better than Chloramphenicol on MIC at 250.0 µg /ml.[7]



Compounds	R	R_1
7 a	CH_3	H
7 b	CH_3	Cl
7 c	C_2H_5	H

Fig: 7

Anti-inflammatory activity:

A series of [(4-Amino 5-Disubstituted-4-H-1,2,4-triazole-3-yl)thio] alkanoic acid derivatives were synthesized by **Kuangsen Sung et al** and .screened for anti-inflammatory activity. Among these derivatives compound **(Fig: 8)** showed significant anti-inflammatory activity. [8]

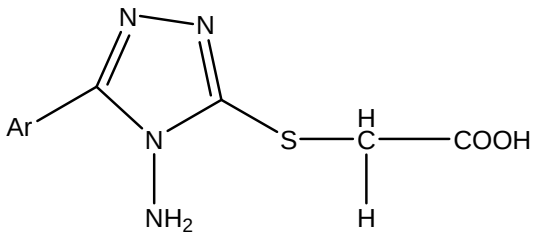
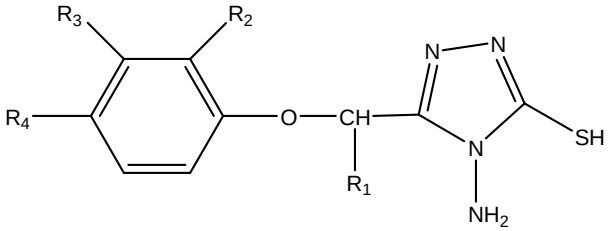


Fig: 8

Prasad et al. synthesized a series of derivatives of [4-Amino-3-Aryloxy alkyl, 5-Mercapto-1, 2,4-Triazole] and evaluated them for anti-inflammatory activity. Out of several compound **(Fig:9)** showed potent anti-inflammatory activity. [9]



Compound	**R_1**	**R_2**	**R_3**	**R_4**
a	H,CH_3	H,CH_3,Cl	H	H, Cl

Fig: 9

Harish Kumar et al synthesized a series of compound 5-[(Biphenyl-4-yloxy)methyl]-4-n-substituents-3-marcapto-(4H)-1,2,4-triazole. Synthesized compounds were screened for anti-inflammatory activity out of the synthesized compounds 5-[(Biphenyl-4-yloxy)methyl]-4-n-butyl-3-marcapto-(4H)-1,2,4-triazole **(Fig:10)** showed potent anti-inflammatory activity.[10]

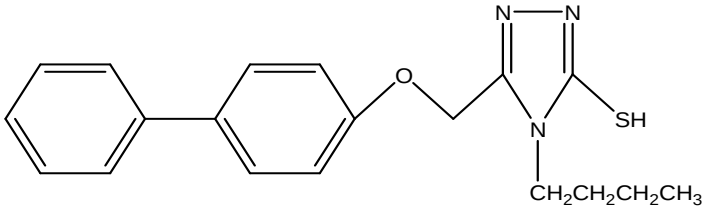


Fig: 10

Anti-cancer activity:

Neslihan Demirbas et al. synthesized a series of compounds 4-amino-3-substituted-5-oxo-4,5--dihydro-[1,2,4] tri-azole-1-yl acetic acid 2 ,4-dichloro-benzylidene-hydrazide derivatives and screened for their anti-cancer activity. The compound **(Fig.11)** 4-amino-3-phenyl-5-oxo-4,5-dihydro-[1,2,4] tri-azole-1-yl acetic acid 2 ,4-dichloro-benzylidene-hydrazide showed a potent therapeutic activity for the treatment of breast cancer.[11]

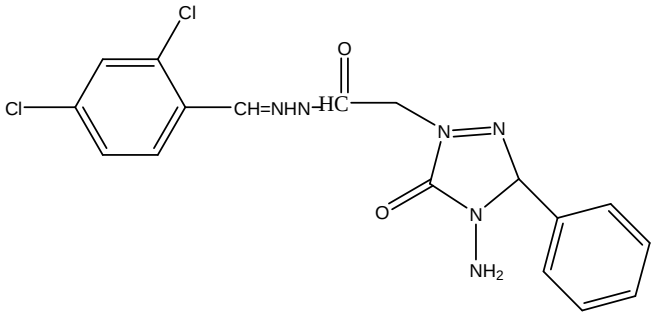


Fig: 11

Analgesic activity:

A series of 5-[(Biphenyl-4-yloxy)methyl]-4-n-substituents-3-mercapto-(4H)-1,2,4-triazole synthesized by **Harish Kumar at al.** Its derivatives such as 5-[(Biphenyl-4-yloxy)methyl]-4-fluorophenyl-3-mercapto-(4H)-1,2,4triazole **(Fig:12)** screened for the analgesic activity.and that compound showed analgesic activity ranging from 16.9% to 72.8%, whereas the standard drug flurbiprofen showed 69.5% inhibition.[10]

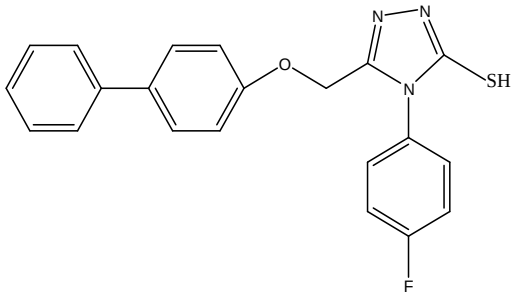
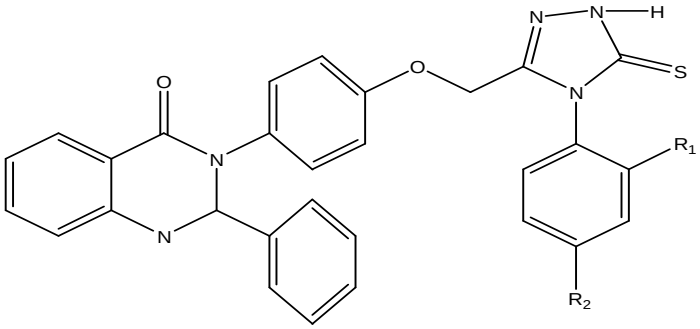


Fig: 12

Antimalarial activity:

Freddy H. Havaldar et al. synthesized a series of derivatives such as 3-[4-(4-substituted phenyl-5-thioxo-4,5-dihydro-1H-[1,2,4]-triazol3ylmethoxy)-phenyl]-2-phenyl-3H-quinazolin-4-ones **(Fig:13)** and screened for anti-malarial activity. Among these derivatives, derivative (b) 3-{4-[4-(4-fluoro-phenyl)-4*H*-[1,2,4]triazol-3-yl-methoxy]-phenyl}-2-phenyl-3*H*-quinazolin-4-one is most active against *strains Plasmodium falciparum*.[4]



compounds	R_1	R_2
13 a	H	H
13 b	H	F
13 c	H	NO_2
13 d	F	F

Fig: 13

Anti-depressant activity:

Mhasalkar et al.synthesized a series of triazole substituted compounds and screened for antidepressent activity. Out of the synthesized compounds **(Fig:14)** 2,4-Dihydro-3H-1, 2,4-triazole-3-thiones showed potential antidepressant activity.[12]

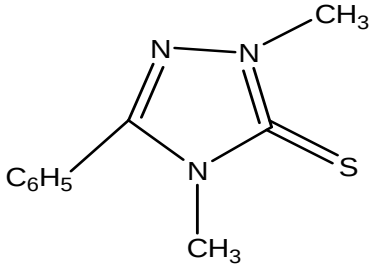


Fig: 14

RESULT AND DISCUSSION

Pharmaceutical chemistry is devoted to the discovery and development of new agents for treating diseases. Inorganic compound continue to be important in therapy, for example as antacids, mineral supplements and radiopharmaceuticals, but organic molecules with increasingly specific pharmacological activities are clearly dominant [13]. The objective of medicinal chemistry is design and the production of compounds that can be use as medicine for the prevention, treatment and cure of humans or animal diseases. It is concerned with the invention, discovery, design, identification of biologically active compounds, the study of their metabolism, interpretation of their mode of action at the molecular level and the construction of structure activity relationship (SAR), the relationship between chemical structure and pharmacological activity for a series of derivatives have been synthesized as target structures and evaluated for their biological activities. The cytotoxicity of the reported compounds in the review indicate good safety associated with many of the triazole derivatives, however, the need for standardized method for cytotoxicity evaluation is required for better understanding of the compounds safety and the safety-structure relationships

CONCLUSION

Triazole is a unique template that is associated with several biological activities. This article highlightened research work of many researchers reported in literature for different pharmacological activities on triazole compounds synthesized. This review has presented comprehensive details of triazole analogues, potent compounds reported for particular pharmacological activity and the method or technique involved in evaluation process. More investigations must be carried out to evaluate more activities of triazole for many diseases whose treatment are difficult in the medical sciences.

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