World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Review Article

Triazoles and its pharmacological activities: A Review

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Received: 07-09-2016 / Revised: 21-10-2016 / Accepted: 23-11-2016 / Published: 26-11-2016

ABSTRACT

Triazole and its derivatives play wide role in drug discovery processes and have considerable chemical significance and biological activities. The triazole derivatives are more than just passive linkers; they readily associate with biological targets, through hydrogen bonding and dipole interactions. In the last years the synthesis of high nitrogen containing heterocyclic nucleus has been attracted to many pharmaceutical industries. Triazole derivatives has a wide range of applications i.e. such as anti-microbial, anti-tumor, anthelmintic, anti-leishmanial, anti-convulsant ,anti-inflammatory, anti-viral, anti-leprotic, anti-depressant, anti-anxiety, antihistamines, antitubercular and analgesic etc. The derivatization of triazole moieties is based on phenomenon of bioisoterism which include replacement of oxygen of oxadiazole nucleus with nitrogen triazole analogue.

Keywords: Triazoles Derivatives, anti-microbial, anti-tumour, anthelmintic, anti-leishmanial, anti-convulsant, anti-inflammatory, and analgesic etc.

INTRODUCTION

In the last very few decades, the chemistry of 1, 2, 4-triazoles as well as their fused heterocyclic derivatives have been receiving considerable attention due to their various synthetic and efficient biological importance. Triazole nucleus have been attracting considerable attention in various field such as medicinal and agrochemical research as well as in material sciences owing to their unique structure and characteristics. The triazoles are said to be the isosters of imidazoles in which the carbon atom of imidazole is isosterically replaced by nitrogen.

Triazoles moieties have been incorporated into a wide range of therapeutically interesting drug molecules including anti inflammatory, sedatives, cns stimulants, antianxiety anti fungal activity and antimicrobial agents. They have been used as optical brightening agents, as antioxidants, as corrosion inhibitors and as additives with a variety of other functions. Many dye stuffs and pigments have heterocyclic compounds. The importance of triazole derivatives lies in the field that these have good position in heterocyclic chemistry, due to its different biological activities Therefore, 1,2,4-triazole derivatives have quite attractive properties and have acquired due attention during the last ew decades.

Biological activities of Triazole derivatives

Triazole derivatives as anti-cancer agents: Cancer is a dreadful disease with a complex pathogenesis, which is threatful for human life greatly. A number of chemotherapeutic drugs have been developed and are being developing to treat cancer including DNA-alkylating agents and antimitotic agents. The current position highlights the need for the discovery and development of new compounds of simple and basic structure, exhibiting optimal *in vivo* antitumor potency, bioavailability and new mechanisms of action. The research for new drugs that can specifically target the tumour cells is today's demand of cancer therapy and is a never ending process, till the goal is achieved.

The successful non-surgical elimination of cancer cells involves apoptosis. The induction of apoptosis by cytotoxic drugs is not only limited to the malignant cells, normal cells are equally vulnerable. So it is necessary to go for new agents that selectively target tumour cells without perturbing normal tissue.

The synthesis of some new compounds and selected to evaluate their *in vitro* growth inhibitory activities against two human cultured cell lines, which are breast carcinoma cell line (MCF7) and

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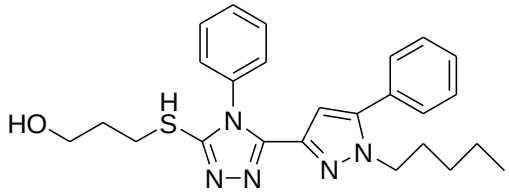
cervix carcinoma cell line (HELA) in comparison to the known anticancer drug, Doxorubicin is taken as a reference drug. It has been noticed from Table 1 that all of the tested compounds showed significant potential antitumor activities. Best results were shown by compound **(1)** 3-{-5-[1-(Aryl)-5-phenyl-1*H*-pyrazol-3-yl]-4-phenyl-4*H*-[1,2,4] triazole- 3-ylthio} propan-1-ol and **(2)** 3-{[(Oxiran-2-yl)methylthio]-5-(1-(aryl))-5-phenyl-1*H*-pyrazol-3-yl}-4-phenyl-4*H*-[1,2,4]triazole.[1,2]

Cytotoxicity of various synthetic compounds of a series of 1, 4-disubstituted 1,2,3-triazoles were performed by Batula *et al.* in three different cell lines (Hep G2, Hela, HL 60 cell lines) Among all the tested compounds phenyl substituent at 4th position- 4-(Phenyl-1-(1- phenyl-ethyl)-1*H*-(1,2,3) **(3)** triazole and α-methyl benzyl group at 1st position-Benzhydryl-4-phenyl-1*H*-[1,2,3]triazole **(4)** exhibited the highest activity against HL 60 cells with IC_{50} values of 1.15 μM. Compound 4 also showed the greatest potency among all against Hela cells with IC_{50} values of 41.40 μM.

Researcher synthesised a series of hybrid 1,3,4-thiadiazoles derivatives possessing γ-substituted butenolide moiety, these chiral 1,2,4-triazole derivatives were tested for their anti-cancer properties towards HeLa cell line and they were found exhibiting good anticancer activities towards HeLa. The compound **(5)** with an IC_{50} of 1.8 μM was found to be the most active. [3.19]

Table 1: Effect of some selected triazole derivatives on MCF7 and HELA tumor cell lines.

Comp.	IC_{50}**{μg/ml}**	
	MCF7	**HELA**
1	2.72	2.98
2	3.63	3.92



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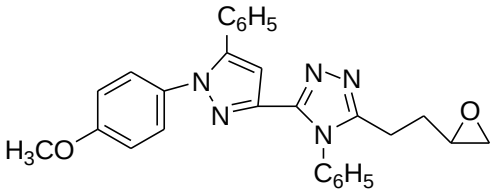

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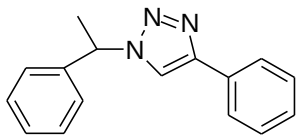
Table 2: Anticancer activities against HELA,HL 60 and HepG2 cell lines

Comp.	HELA Cell Line	HepG2 cell line	HL 60 cell line
	IC_{50} μM	IC_{50} μM	IC_{50} μM
3	41.40	278.75	1.15
4	148.12	No activity	201.10



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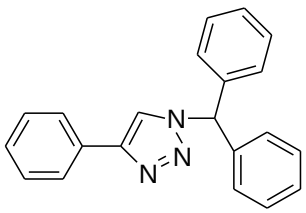

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Table 3: In vitro anticancer activities against HeLa cell lines with compounds

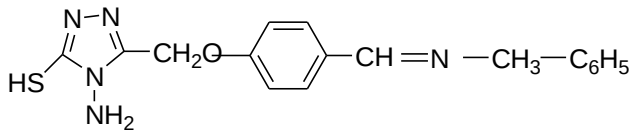
Comp.	IC_{50} **(μM)**
5	1.8
DDP (Cisplatin)	2.6

Triazole derivatives as anti-inflammatory agents: Prostaglandins are endogenous substances which are involved in various processes of physiological nature and are effective mediators of inflammation. Prostaglandins are produced, together with other prostanoids, in the arachidonic acid metabolism, whose first step, consisting of the oxidative conversion of arachidonic acid into prostaglandin H2, is being catalyzed by cyclooxygenase (COX). This enzyme exists basically in two isoforms, one constitutive (COX-1) and the other inducible (COX-2). Most of the non-steroidal anti-inflammatory drugs (NSAIDs) have their action by reducing prostaglandin biosynthesis by inhibiting COX reaction. The triazole derivatives were screened for anti-inflammatory activity using rat hind paw method of Winter *et al*, modified by Dhawan and Srimal as well as screened for their analgesic activity. Anti-inflammatory activity carried out by carrageenan induced rat paw oedema method showed that triazole derivatives of both mono substituted amines and acid hydrazides possessed significant anti-inflammatory activity comparable to standard drug (Ibuprofen). [4,5]

Eight new compounds of triazole moiety were synthesised by Pattan *et.al*. And all of these compounds were screened for their anti-inflammatory activity. Out of the eight compounds, the compounds which possessed the good anti-inflammatory activity were found to be **(8-9)** .The anti-inflammatory activities of the compounds 8 and 9 as found by the screening test were satisfactory and are shown at an interval of 1 hr each and their %inhibition are being calculated for analysing their anti-inflammatory activities. The anti-inflammatory activities of the compounds are shown as follows in the table 5. Carrageenan induced rat paw oedema method was employed for evaluating the anti-inflammatory activity of synthesized compounds by Kumudha *et al*.and were given intra-peritonially at the dose of 50mg in albino rats using diclofenac sodium as a standard drug.Out of the various compounds (**10-14)** were found to possess significant anti-inflammatory activity at an interval of 4 hrs.The anti-inflammatory activities of the compounds showing satisfactory results of the following compounds are shown in the following table 6. [6]

Table 4: Anti-inflammatory activity of triazole derivatives

Comp.	OedemaVol. (ml)	% red.	Oedema Vol. (ml)	% red.	Oedema Vol. (ml)	% red.	Oedema Vol. (ml)	% red.
6	0.5583 ±0.0247	20	0.5166 ±0.032	42	0.450 ±0.0288	58	0.435 ±0.026	68
7	0.5583 ±0.0247	19	0.505 ±0.029	43	0.445 ±0.0325	59	0.426 ±0.032	69
Control	0.6916 ±0.2712	-	0.895 ±0.018	-	1.091 ±0.481	-	1.425 ±0.613	-
Streptomycin	0.415 ±0.0214	39	0.343 ±0.029	61	0.320 ±0.0275	70	0.2966 ±0.024	80



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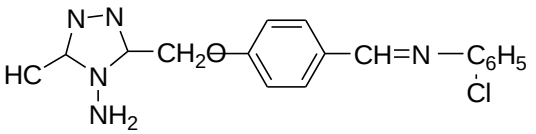

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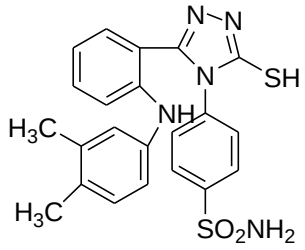
Table 5: Anti-inflammatory activity of triazole derivatives

Comp.	0 hr	1 hr	2 hr	3 hr	4 hr	%inhibition
8	0.975	1.475	1.650	1.775	1.842	38.62
9	0.975	1.225	1.325	1.350	1.275	44.47
Control	0.975	1.400	1.425	1.550	1.425	40.26
Std.	1.060	1.375	1.435	1.440	1.320	39.54



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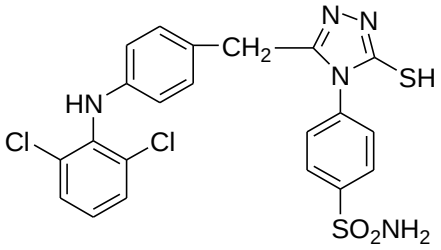

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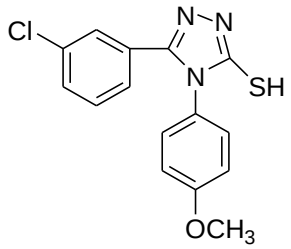
Table 6: Anti-Inflammatory Activity Of Compounds (10-14)

Comp.	NORMAL PAW VOLUME	PAW VOLUME AFTER 4HRS
10	0.35 □□0.027	0.38 □□0.022
11	0.24 □□0.005	0.33 □□0.016
12	0.27 □□0.001	0.32 □□0.006
13	0.23 □□0.001	0.26 □□0.007
14	0.23 □□0.009	0.22 □□0.004
Control	0.25	0.60 □□0.013
Std.	0.24 □□0.017	0.43 □□0.014



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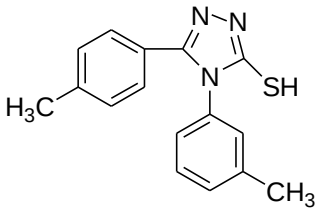

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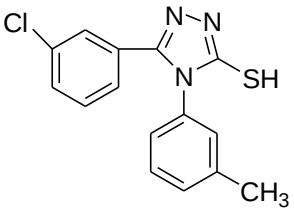

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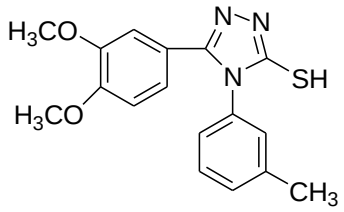

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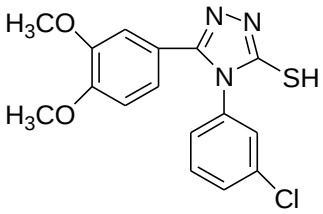

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Triazole derivatives as antimicrobial agents: There is no doubt in the context that the existing arsenal of antimicrobial agents which we are having in our hands for the treatment of infectious diseases will be insufficient over the coming decades. The primary reason for this is the inexorable drive of evolution leading to antimicrobial resistance culminating with the failure of current treatments. Fungal infections requires special attention as fungi are emerging as important nosocomial pathogens and reason for causing severe morbidity and mortality in immune compromised patients. Modern therapies and management such as bone marrow or solid-organ transplants, and much new aggressive chemotherapy have resulted in a rapidly expanding number of immunosuppressed patients. These patients now survive longer than before and have become more susceptible to life-threatening fungal infections. Concomitant with the increased incidence of fungal infections has been a dramatic increase in the use of antifungals for the treatment of both systemic and localized fungal infections. So, in order to meet above mentioned challenges, there is an urgent requirement for the development of novel antimicrobial agents. Subageetha synthesized new compounds Certain 3-pyridyl [1,2,4] triazolo [3,4-*b*] [1,3,4] thiadiazepines and they were screened for their *in vitro* antibacterial activity. *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Escherichia coli* were used to determine anti-bacterial activity. Compounds **(15)** 6-(4-Cl phenyl)-8-(*N*-3,4,5-Tri methoxy phenyl)-3-(pyridin-yl)[1,2,4] triazolo

[3,4-*b*][1,3,4] thiadiazepine & **(16)** 6-(Br- phenyl)-8-(*N*-2,4-Di- chloro phenyl)-3-(pyridin-yl)[1,2,4] triazolo [3,4-*b*][1,3,4] thiadiazepine were found to be most potent against *Bacillus subtilis* and *Staphylococcus aureus* respectively.[7]

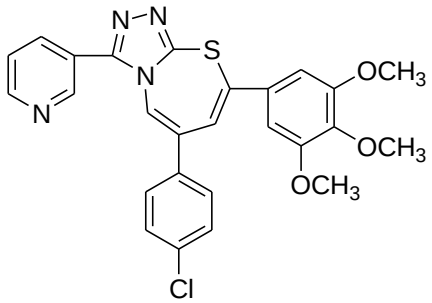
Bhagyalakshmi *N* synthesised the different Novel Triazole schiff bases derivatives and they were screened for *invitro* antibacterial activity against the standard strains of *Staphylococcus aureus, Bacillus subtilis* (Gram positive), *Escherichia coli* and *Pseudomonas auriginosa* and it was observed that the compounds derived from acid hydrazides like **(17)** 4-amino-3-2(4-isobutyl phenyl) propionyl carboxamido -5-mercapto-1,2,4-triazoles and **(18)** 4-amino-3-2(5-methoxy naphthyl) propionyl carboxamido -5-mercapto-1,2,4-triazoles were found to possess much higher activity than triazole derivatives derived from aromatic amines as shown in table 8.[8]

Abdulrasool *et al* synthesised different compounds and the antibacterial test was performed according to the disc diffusion method.Compounds (**19-22)** were assayed for their antimicrobial activity *in vitro* against four strains of bacteria (two of them were gram negative (*Escherichia coli, Klebsiella pneumoniae*) From the result, we conclude that the compounds **(19)** 5,5'-methylenebis(4-amino-4*H*-1,2,4-triazole-3-thiol),**(20)**bis(6-(4-bromophenyl)-7*H*-[1,2,4]triazolo[3,4 *b*][1,3,4]thiadiazin-3-yl)methane**, (21)** 4[amino]-5-phenyl-4H-1,2,4-triazole-3-thiol and **(22)** 6-(4-bromophenyl)-3-phenyl-7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazine have good biological activities as is clear from the table 9.[9]

Table 7: In vitro antibacterial activity of the compounds

Comp.	**Zone of inhibition in mm**			
	***Bacillus subtilis* NCIM 2010**	***Staphylococcus aureus* NCIM 5021**	***Escherichia coli* NCIM 2911**	***Pseudomonas aeruginosa* NCIM 5029**
15	19	13	12	-
16	13	20	14	-
Standard (Ciprofloxacin) 5 mcg/disc	29	31	29	30

(-) Indicates no zone of inhibition
Zone of inhibition : <12 mm categorized as Resistant
12-18 mm categorized as Moderately Sensitive
>18 mm categorized as Sensitive



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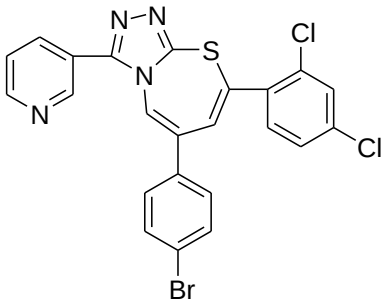

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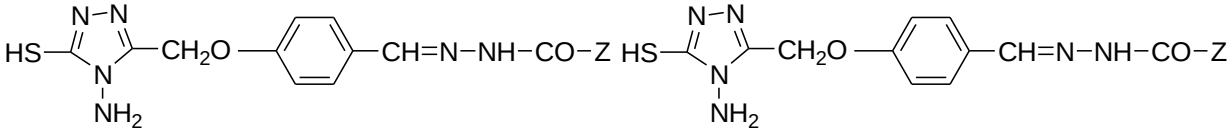
Table 8: Antibacterial activity of triazole derivatives

Comp.	Antibacterial activity zone of inhibition in mm and concentration in µg/ml.							
	S. aureus		*B. subtilis*		*E. coli*		*P. aeruginosa*	
	100	200	100	200	100	200	100	200
17	6	12	7	14	8	13	7	13
18	7	14	8	15	7	16	6	12
Control	0	0	0	0	0	0	0	0
Streptomycin	12	20	8	18	20	32	18	26
Ampicillin	12	22	10	18	14	20	12	22



Z=2(4-isobutyl phenyl)propionyl carboxamido
17

Z=2(5-methoxynaphthyl)propionyl carboxamido
18

Table 9: Inhibition zones of compounds (19-22) and the references antibiotics

Comp.	Zone of inhibition in mm				
	Concentration mg/mL	***E.faecalis***	***S.aureus***	***E.coli***	***K.pneumonia***
19	25	15.8	18.94	18.9	17.2
20	25	16.77	17.58	15.39	16.17
21	25	15.5	17.9	16.22	15.9
22	25	19.3	18.26	23.77	16.8

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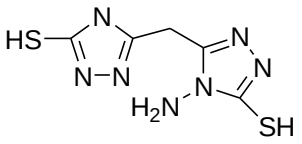

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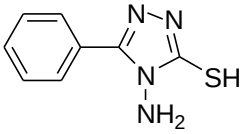

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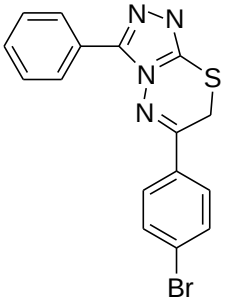

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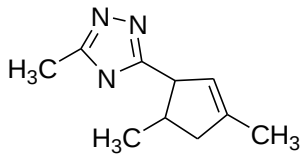
All newly synthesized compounds 3-Alkyl-5-substituted 1,2,4-triazole derivatives by Ramesh kumar *et al.* were evaluated for *in vitro* antibacterial activity against gram positive and gram negative bacterial strains such as *Escherichia coli, Pseudomonas aeruginosa*, *Strophylococcus aureus* and *Streptococcus pyrogenes* **(23)** 3-alkyl-5-(3',5-dimethyl-1-*H*-pyrazole-1-yl)-1,2,4-triazole and **(24)** 3-alkyl-5-(*N*-pyrazolidine)-amino-1,2,4-triazole exhibited best activity as shown in the table 10. Abdulrasool *et al* synthesised different compounds and evaluated for their anti-fungal properties and it was found that compounds **(25)** 5,5'-methylenebis(4-amino-4H-1,2,4-triazole-3-thiol), **(26)** 4[amino]-5-phenyl-4*H*-1,2,4-triazole-3-thiol **(27)** 6-(4-bromophenyl)-3-phenyl-7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazine shows biological activity as antifungal agents against *Candida Albicans* higher than fluconazole this may attributed to S-H for compounds 25,26 and thiadiazoline ring for compound 27.The anti-fungal activity is shown in the table 11.[9]

Banday *et al*. synthesised unsymmetrical bis-1,2,3-triazoles. The fungal strains used were *Aspergillus niger* and *Penicillium chrysogenum* .Different compounds were synthesised and were evaluated for their anti fungal properties and it was found that the compounds **(28)** 1-(4-methoxyphenyl)-5-(2-(1-p-tolyl-1*H*-1,2,3-triazol-4-yl)ethyl)-1*H*-1,2,3-triazole and **(29)** 1-(3-nitrophenyl)-5-(2-(1-m-tolyl-1*H*-1,2,3-triazol-4-yl)ethyl)-1*H*-1,2,3-triazole were found to be more potent.[10]

Table 10: Antibacterial activity of compounds (23-24) in terms of diameter of inhibition zone in mm

Comp.	Zone of inhibition in mm			
	E. coli	***P. aeruginosa***	***S. aureus***	***S. pyrogenes***
23	12	15	14	18
24	13	19	13	16
Ciprofloxacin	24	24	25	22



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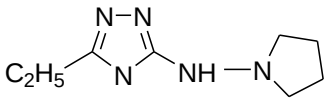

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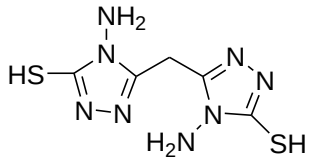
Table 11: Inhibition zones of compounds (25-27) and the references antifungal

Comp.	Zone of inhibition in mm	
	Concentration (mg/ml)	**Candida Albicans**
25	25	17.85
26	25	16.89
27	25	22.73
Fluconazole	25	17.58



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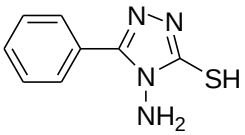

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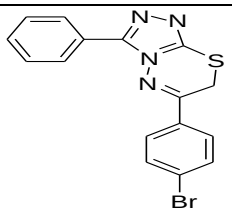

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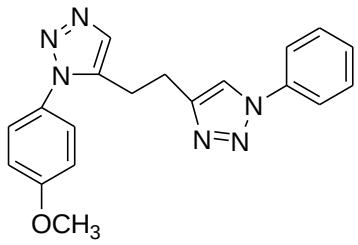
Table 12: Zone of inhibition in mm of different anti fungal agents

Comp.	Zone of inhibition in mm	
	A.niger	***P.chrysogenum***
28	12	12
29	13	14
Fluconazole	18	14



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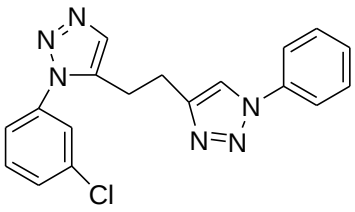

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Triazole derivatives as Anti-oxidant Agents: Oxidation processes are intrinsic to the energy management of all living organisms and are therefore need to be kept under strict control by several cellular mechanisms. Antioxidants are very important compounds that help in reducing or neutralizing the free radicals, and thus protecting the cells from oxidative injury. Free radicals are the molecules or ions or atoms which are having unpaired electrons in their outermost shell of electrons. These species which are being constantly formed in human body, may become toxic when generated in excess or in the presence of a deficiency in the naturally occurring antioxidant defences Therefore, considerable research has been directed towards the formation of new antioxidants to prevent radical-induced damage.

The free radical scavenging activity of all compounds of Hydrazinecarbothioamide and 1,2,4-triazole class containing diarylsulfone and 2,4-difluorophenyl moieties was carried out by Saramet *et.al*.in the presence of the stable free radical (1,1-diphenyl-2 picrylhydrazyl) DPPH using ascorbic acid (AA), *tert*-butyl-4-hydroxyanisole (BHA) and 2,6-bis(1,1-dimethylethyl)-4-methylphenol (BHT) antioxidant agents as positive control. Based on the experimental results, among all the compounds synthesized, hydrazinecarbothioamides **(30)** 2-(4-(4-X-phenylsulfonyl) benzoyl)-*N*-(2,4-difluorophenyl) hydrazinecarbo-thioamides showed higher scavenging activity towards DPPH.

Novel triazole-thiol and thiadiazole derivatives of the 1,2,4-Triazole-3(5)-one Class were obtained by Sancak *et.al*.and were evaluated for their anti-oxidant activity and out of the various compounds *N*-(4-Halo/methyl- phenyl)-2-(2-(4-(4-(1-(2-(2-(4-halo/methyl phenylcarbamothioyl)hydrazinyl)-2-oxoethyl)-3-methyl-5-oxo-1*H*-1,2,4-triazole-4(5*H*)-yl)alkyl)-3-methyl-5-oxo-4,5-dihydro-1,2,4-triazole-1-yl)acetyl)hydrazinecarbothioamides **31-32** were found to possess remarkable activity. Some benzotriazole substituted with N-phenylacetamide and acetylcarbamic acid derivatives were synthesized by Jamkhandi *et al* and antioxidant activity was reported Present study was focused on evaluation of 2-(1*H*-1,2,3-benzotriazol-1- yl)-*N*-phenylacetamide and [(1*H*-benzotriazol-1-ylacetyl)amino]acetic acid derivatives for antioxidant activity. The derivatives like **(33)** 2-(1*H*-benzotriazol-1-yl)-*N*-(4-sulfamoyl phenyl) acetamide, **(34)** 2-(1*H*-benzotriazol-1-yl)-*N*-(4-hydroxyphenyl) acetamide and **(35)** 2-[(1*H*-benzotriazol-1-ylacetyl)amino]propanoic acid showed remarkable Scavenging activity when compared to ascorbic acid.[10,11]

Table 13: Antioxidant activity of compound 30 by DPPH method.

Comp.	Scavenging Effect (%)						IC_{50} (μM)
	Conc. 25 μM	**Conc. 50 μM**	**Conc. 75 μM**	**Conc. 100 μM**	**Conc. 125 μM**	**Conc. 250 μM**	
30	30.54±1.32	64.37± 1.35	74.86±1.40	85.39±1.45	95.99±1.50	97.18±1.42	39.39
AA	0.70 ± 1.00	1.08 ± 0.84	17.48±1.03	34.91±0.69	84.12±0.48	91.26±0.49	107.67

AA=Ascorbic acid

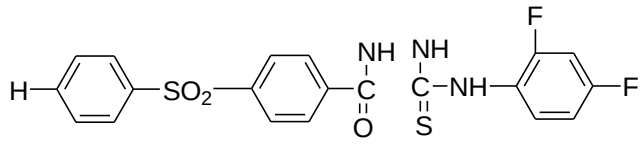

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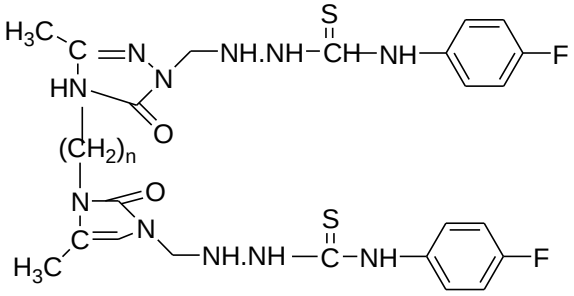
Table 14: IC50 values of compounds 31 and 32

Comp.	DPPH IC_{50} (μg/mL) ± 0.5
31	4.7 ± 0.7
32	4.1 ± 0.5
BHT (Positive control)	19.8 ± 0.5

BHT: Butylated Hydroxy Toluene



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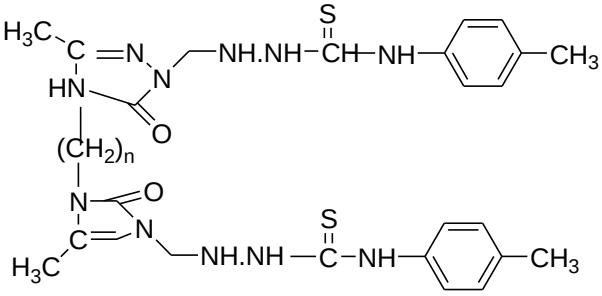

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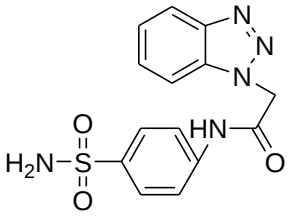
Table 15: Antioxidant activity of Benzotriazole derivatives

Comp.	Conc. 25µg/ml	Conc. 50µg/ml	Conc. 75µg/ml	Conc. 100µg/ml	Average	STDEV	SEM
33	43.57143	55.10949	50.27473	62.42424	52.84497	7.947646	±3.973822
34	47.68212	53.7594	50.54645	61.49068	53.36966	5.955992	±2.977996
35	42.12454	53.23194	49.1573	61.00629	51.38002	7.888789	±3.944394
Ascorbic	48.02632	55.7554	53.82653	64.77273	55.59524	6.944274	±3.472137



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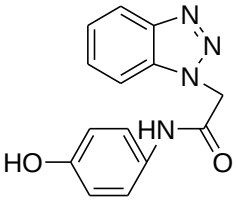

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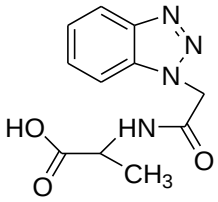

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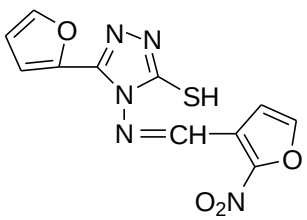
Triazole derivatives as ET Receptor Antagonist:
A endothelin receptor antagonist (ERA) is a drug that blocks endothelin receptors.
Three main kinds of ERAs exist:

- Selective ET_A receptor antagonists (sitaxentan, ambrisentan, atrasentan, BQ-123, zibotentan), which affect endothelin A receptors.
- Dual antagonists (bosentan, macitentan, tezosentan), which affect both endothelin A and B receptors.
- Selective ET_B receptor antagonists (BQ-788 and A192621) which affect endothelin B receptors are used in research but have not yet reached the clinical trial stage.

Scientists are carrying on researches on triazole moieties to find their potent antagonist activities.
Xin Yong *et al* prepared a series of 4-Amino-5-furyl-2-yl-4*H*-1, 2, 4-triazole-3-thiol derivatives and assayed for their Endothelin(ET) Receptor Antagonists by using the cell culture solution of the rat heart ventricle muscle membranes. Compound **(36)** represented a new leading compound of ET receptor antagonist which exhibited high inhibition of 71.93%.[12]



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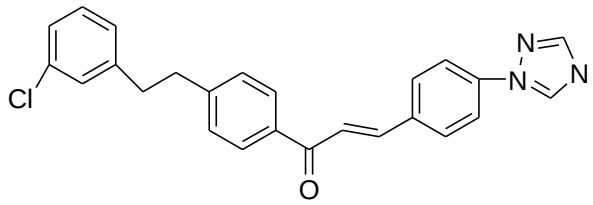
Triazole derivatives as Antitubercular Agents: Tuberculosis (TB) is an infectious disease which is caused by the bacillus *Mycobacterium tuberculosis* (MTB). It is the most dangerous bacterial infection responsible for drastic increase in death cases. The tubercle bacillus was discovered by Robert Koch in 1882.

Tuberculosis is a chronic granulomatous infectious disease. Infection may occur due to presence of aerosol, and inhalation of a few droplets containing *M. tuberculosis* bacilli. After infection, *M. tuberculosis* pathogenesis usually occurs in two stages. The first stage is an asymptomatic state which may persist for several years in the host, which is called latent TB. When the immune system is weak, the bacteria starts replicating and cause characteristic symptoms such as cough, chest pain, fatigue and unexplained weight loss. If this is left untreated, the disease may eventually culminate in death. MDR-TB is defined as the resistance of the bacilli to isoniazid and rifampicin, with or without resistance to other first-line drugs. XDR-TB is defined as resistance to at least isoniazid and rifampicin, or to any fluoroquinolone, or to any of the three second-line injectables (amikacin, capreomycin, and kanamycin). It has been researched and found that 3.7% of new patients and 20% of previously treated patients are suffering from MDR-TB. Thus there is an urgent need for discovering new drugs to treat tuberculosis with special emphasis on shortening the regimen than the current drugs and as well as novel pathway for mechanism of action to treat MDR-TB.

Marrapu *et al*. have reported the synthesis of triazoles derivatives. Ten compounds have exhibited good antitubercular activity with MIC in the range of 3.12- 0.78 ìg/mL Most of the compounds with potent in vitro activities were found non-toxic against VERO cell line and mouse derived macrophages. One compound showed good ex-vivo activity with 99% **(37)** inhibition of growth of intracellular bacilli.

Foks *et al*. have synthesized triazole derivatives which were found to possess antitubercular activity in the range 25–100 μg/mL. N-substituted triazoles **(38)** were found to possess activity against Mtb lesser than the S-substituted triazoles. Thus indicating that substitution at sulphur is preferred than at ring nitrogen in 1,2,4-triazoles. Triazolyl imidazoles **(39)** synthesized by Jadhav *et al*., possessed MIC less than 6.25μg/ml against *Mycobacterium tuberculosis*.[13]

Kini *et al*., have reported the synthesis and evaluation of antitubercular activity of 1,2,4-triazoles. Two of them **(40,41)** possessed antitubercular activity at 1 μg/mL.[14-15]. Joshi *et al.* have reported synthesis of 5-substituted-4-amino-1,2,4-triazolin-3-thione **(42)** with moderate antitubercular activity.[16]



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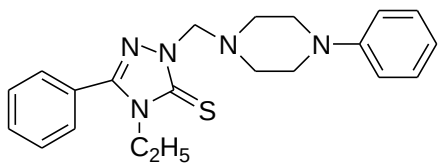

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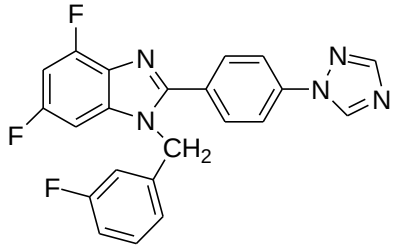

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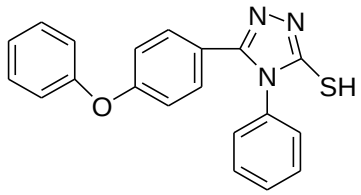

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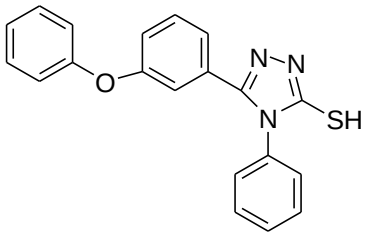

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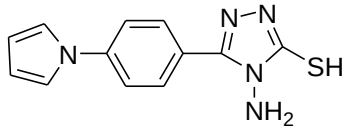
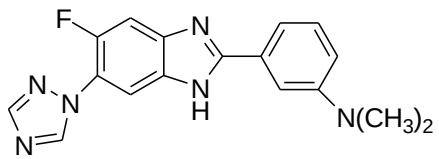


42

Three different series of compounds of new imidazole and 1,2,4-triazole substituted fluorobenzimidazoles were synthesized and screened against M.tuberculosis H37Rv by MABA method by Nandha *et al.* The azole substituted fluorobenzimidazoles displayed antitubercular activity with MIC ranging from 12.5 to >100 µg/mL and the results of antitubercular activity are repoted in Table 1. Among the compounds having 4-chloro, 4-dimethyl amino and methoxy substituent in aromatic ring, compounds with dimethyl amino subtituent **(43)** 4-(5-fluoro-6-(1*H*-1,2,4-triazol-1-yl)-1*H*-benzo[d]imidazol-2-yl)-*N*,*N*-dimethylbenzenamine and **(44)** 4-(5-fluoro-6-(1*H*-imidazol-1-yl)-1*H*-benzo[d]imidazol-2-yl)-*N*,*N*-dimethylbenzenamine were more active with MIC of 25 µg/mL.[17]

Table 16: Antitubercular activities of compounds (43-44) against M.tuberculosis H37Rv

Comp.	MIC (µg/ml)
43	25
44	25
Isoniazid	0.65



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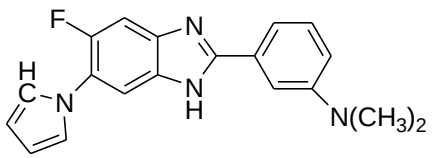

44

Triazole derivatives as anti- convulsant agents: Epilepsy is not a disease, but it is a syndrome of different cerebral disorders of the central nervous system of brain characterized by paroxysmal cerebral dysrhythmia, manifesting as brief episodes (seizures) of loss or disturbances of consciousness, with or without characteristic body movements called convulsions. Many patients have suffered and are suffering from seizures that are resistant to available medical therapies. The convulsions of approximately 25% of epileptics are inadequately controlled by standard drug therapy. The number of drugs useful for the treatment of epilepsy is very small. In an attempt to develop anticonvulsant agents we have tested various five membered heterocyclic compounds and which have showed significant anticonvulsant activities. Triazoles have also attracted much attention due to their significant anticonvulsant activity. Some Coumarin incorporated triazoles 3-(4-{[(substituted phenyl) methylidene]amino}-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-2*H*-chromen-2-ones were synthesised by Mashooq *et al*. Among these, compound **(45)** 3-(4-{[(fluorophenyl) methylidene] amino}-5-thioxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-2*H*-chromen-2-ones showed protection from seizures at the lowest dose (30 mg/kg) after 0.5 h.[18,20]

Some of the selected compounds namely substituted 4,5-diphenyl 4*H*-1,2,4-triazole-3-thiols by Kumudha *et al.* and were screened for anticonvulsant activity. The principle is being supramaximal electric shock method compounds **(46)** 3- methyl-4-methoxy-4,5-diphenyl 4*H*-1,2,4-triazole-3-thiols**, (47)** 3-methyl-4-chloro- 4,5-diphenyl 4*H*-1,2,4-triazole-3-thiols**, (48)** 3,4-dimethoxy-4-methyl-4,5-diphenyl 4*H*-1,2,4-triazole-3-thiols were found to possess good anticonvulsant activity.[6]

Table 17: Anticonvulsant activity and minimal motor impairment of compounds

Comp.	Intraperitoneal injection in mice				Neurotoxicity screen	
	MES		scPTZ			
	0.5 h	4.0 h	0.5 h	4.0 h	0.5 h	4.0 h
45	30	100	100	300	-	-
Phenytoin	30	30	-	-	100	100
Ethosuximide	-	-	300	-	-	-
Carbamazepine	30	-	100	-	100	300
Valproic acid	-	-	300	-	-	-

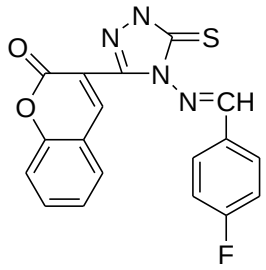

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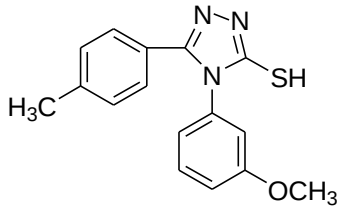
Table 18: Anticonvulsant Activity of the Compounds

Comp.	DURATION OF EXTENSION PHASE IN SEC (Mean ± SEM)
46	6.33±0.477
47	2.25 ± 0.381
48	6.33±0.44
Control	12.83 ± 0.714
Std.	2.25 ± 0.381



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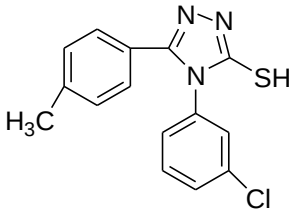

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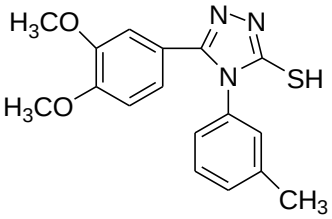

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Conclusion

Summarizing, after review of literature reports described above we can say that triazoles and its derivatives do constitute an important class of medicinal compounds having diverse spectrum of biological activities *i.e.* anticancer, antimicrobial, anti-inflammatory, antifungal and anticonvulsant activities which have created interest among researchers and scientists to synthesize various types of derivatives which are having immense potential to be investigated for newer therapeutic possibilities.

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