Review Article

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Triazole: A Potentially Biologically Attractive Scaffold

Asif Husain*, Md Azhar Iqbal*, Ozair Alam*, Aftab Ahmad, Shah Alam Khan***, Anwar Ali Mohammad Alghamdi****

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Abstract

Triazoles are five-member nitrogen containing heterocyclic compounds. Triazole derivatives have great importance in the field of chemical synthesis, agriculture and pharmaceutical industries due to their wide range of applications. Over the past few decades, researchers have focused their research on the synthesis of novel triazole derivatives. The 1,2,4-triazole heterocyclic ring is an integral part of various synthetic compounds with wide range of therapeutic and pharmacological potentials like anti-inflammatory, antibacterial, anticancer, antifungal, antiviral, anticonvulsant, anti-tubercular, etc. Many marketed drugs are triazoles derivatives like antifungal drugs which include fluconazole, ravuconazole, itraconazole, and voriconazole. Due to the wide scope of pharmacological potentials of triazole derivatives, research community has shown great interest to discover triazoles having potent bio-activities with lesser side effects. This review summarizes the recent developments on the synthetic approaches, mechanism of action, and pharmacological properties of latest and novel triazole derivatives.

Keywords: Nitrogen Heterocycles; Azole; Synthesis; Antimicrobial.

Author Affiliation: *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi 110 062, India. **Health Information Technology Department, Jeddah Community College, King Abdulaziz University, Jeddah-21589, KSA. ***Dept of Pharmacy, Oman Medical College, PO Box 620, PC 130, Muscat, Oman.

Reprint Request: Asif Husain, Associate Professor, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hamdard University, New Delhi-110 062, India.
E-mail: drasifhusain@yahoo.com, ahusain@jamiahamdard.ac.in

Introduction

In current scenario, researchers from all over the word seem to have focused their research to study novel and safer therapeutic agents which can be used clinically. Triazole is an important five member aromatic heterocyclic compound with molecular formula $C_2H_3N_3$ having two carbons and three nitrogen atoms. It occurs as three different tautomers. Numerous nitrogen containing heterocyclic compounds are available as therapeutic agents. In general azole nucleus has been used to treat fungal infection of humans, animals, and plants.

Generally nitrogen containing heterocyclic molecule have various applications in medicinal chemistry. Numerous nitrogen containing heterocyclic compounds are available as therapeutic agents. The examples of triazole containing antifungal drugs are itraconazole, fluconazole, isavuconazole, posaconazole, pramiconazole, voriconazole, and examples of the triazole containg fungicides are cyproconazole, metconazole, epoxiconazole, triadimenol, propiconazole, etc. Triazoles are very important and unique group of nitrogen containing heterocyclic agents. Due to the precursor of large number of biologically active heterocyclic compounds, triazole derivative has tremendous use in medicinal chemistry. It is well known from the literature that the compound 1,2,3-triazole,1,2,4-triazole and 1,3,4-triazole possess wide

range of biological and pharmacological properties [1], like antibacterial [2-4], antitubercular [5,6], anticancer [7-12], antimalarial [13], antifungal [14], anticonvulsants [15], anti-inflammatory [16,17], anticholinesterase [18], antileishmanial [19], antiallergic [20], antioxidant [21], antiHIV [22,23], antiviral [24] and antimicrobial [25]properties.

Triazoles are five member rings having two carbon and three nitrogen atoms. There are the two isomers of triazole which includes 1,2,3-triazole and 1,3,4-triazole. These isomers exist in tautomeric forms based on the position of hydrogen atom [24-31] (Figure 1).

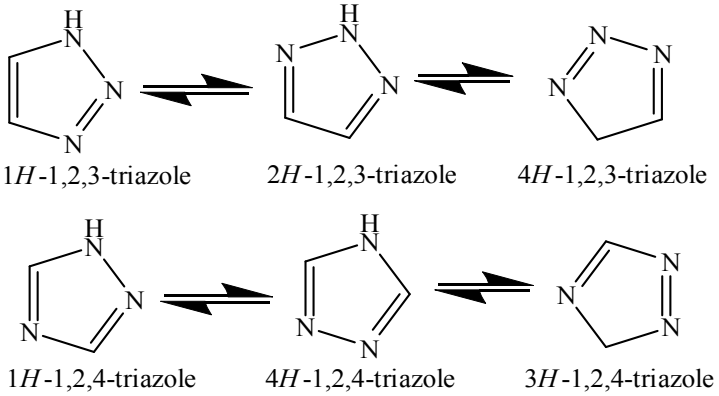
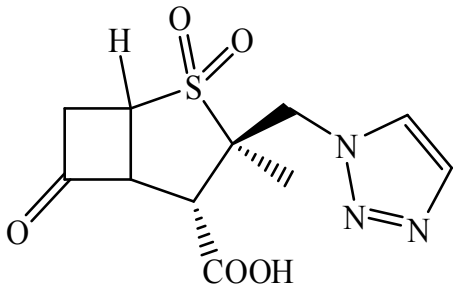
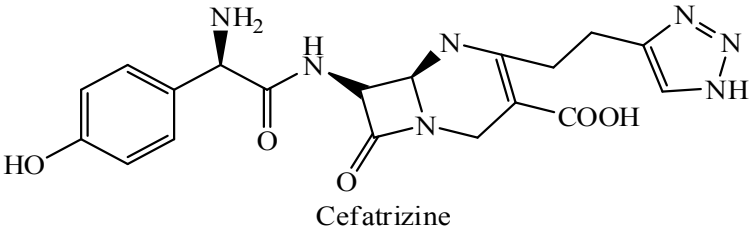


Fig. 1: Tautomers of 1,2,3 triazole and 1,2,4 triazole

Several currently available drugs containing triazole nucleus are used for different clinical conditions [27-29] (Figure 2).



Tazobactum
1



Cefatrizine
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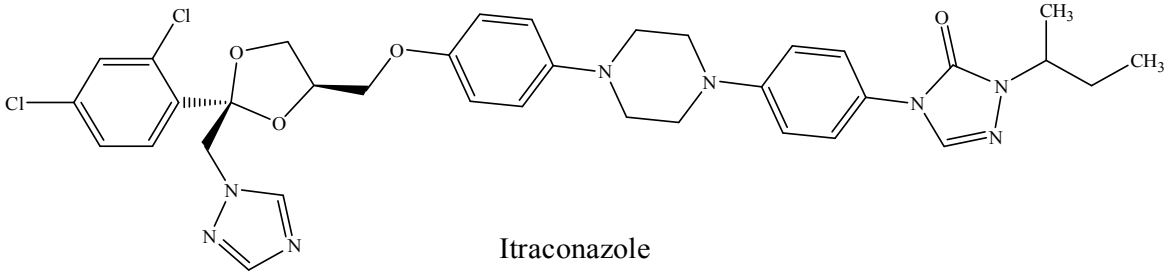

Itraconazole
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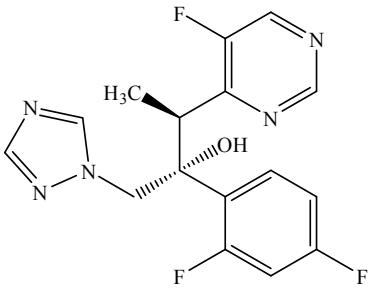

Voriconazole
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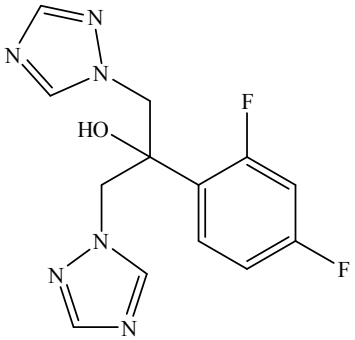

Fluconazole
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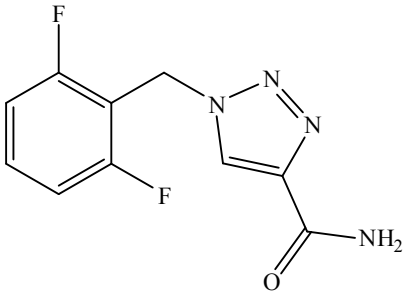

Rufinamide
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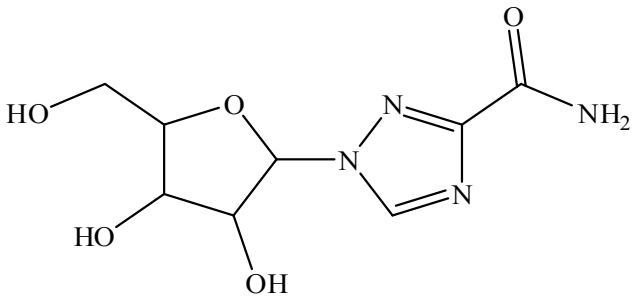
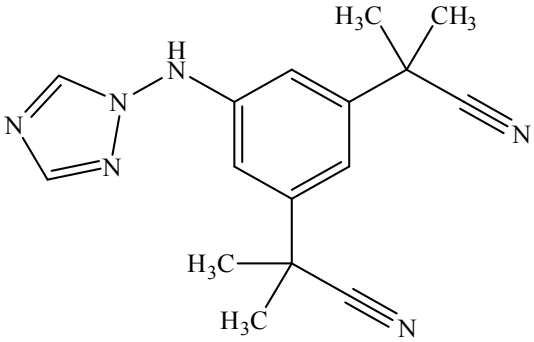


Ribavirin
7



Anastrozole
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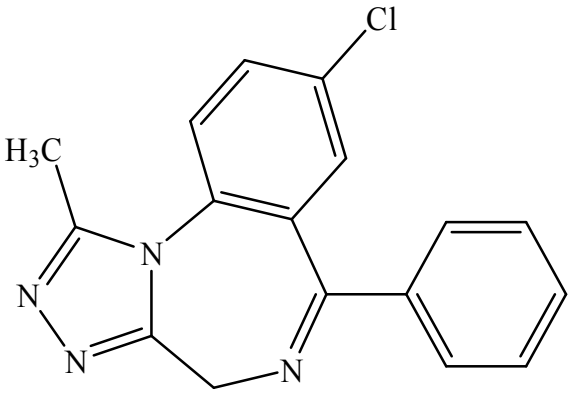

Alprazolam
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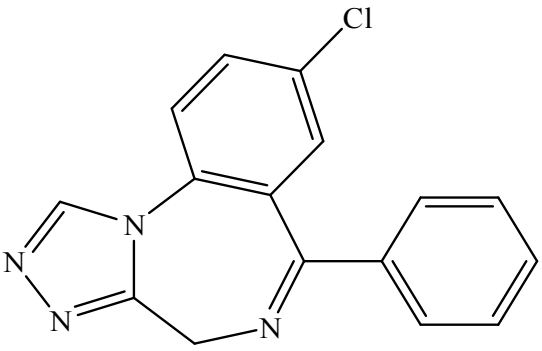

Estazolam
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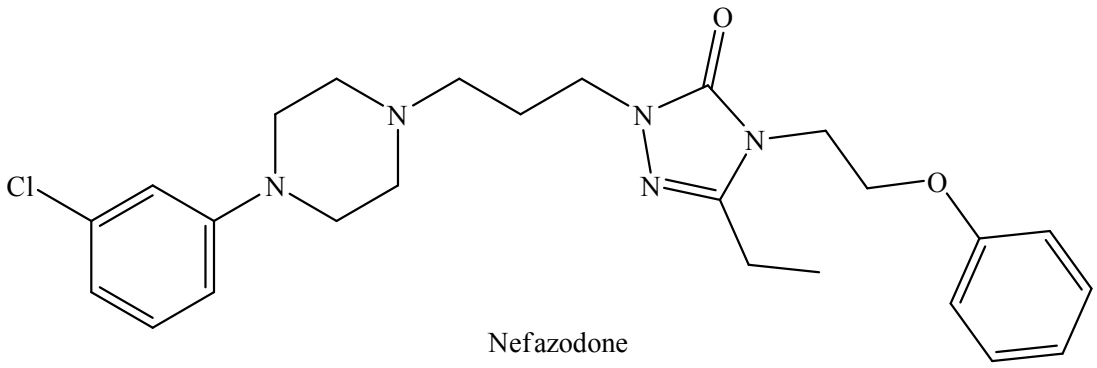


Nefazodone

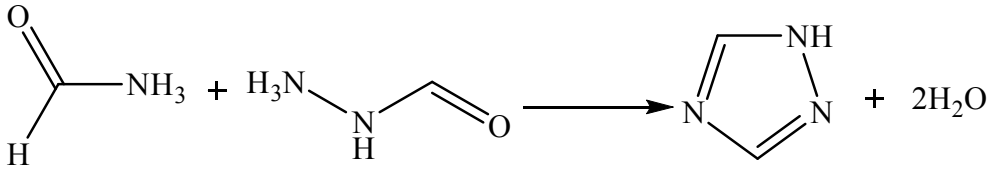
11

Fig. 2: Chemical Structure of Currently available drugs containing triazole nucleus

Chemistry

Preparation of Triazoles

i) Triazoles may be prepared by heating acid hydrazide with amides e.g. formyl hydrazide and formamide give triazole [24][**12**].



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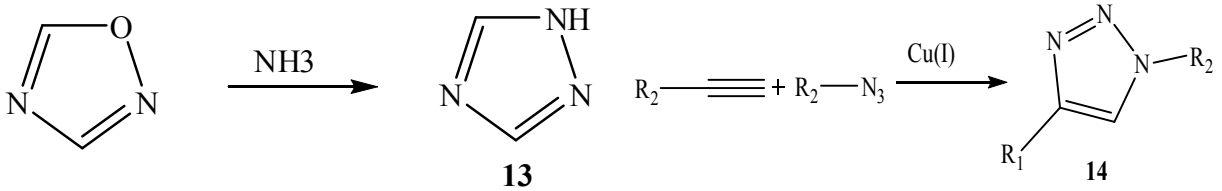
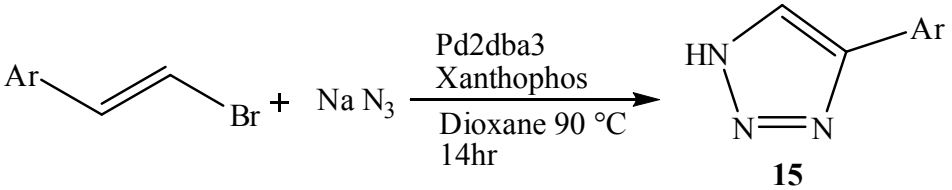
ii) 1,2,4-oxadiazoles give triazoles [**13**] in presence of ammonia [24].

iii) 1,2,3-triazole moiety [**14**] is obtained from cycloaddition of azide and terminal alkyne. This special cycloaddition is called Huisgen cycloaddition [27].



13 **14**

iv) Formation of 1,2,3-triazole [**15**] by the reaction of alkenyl halide and sodium azide in the presence of palladium [27].



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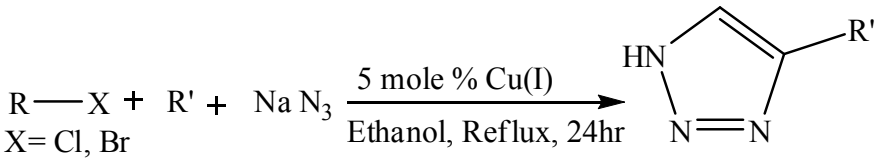

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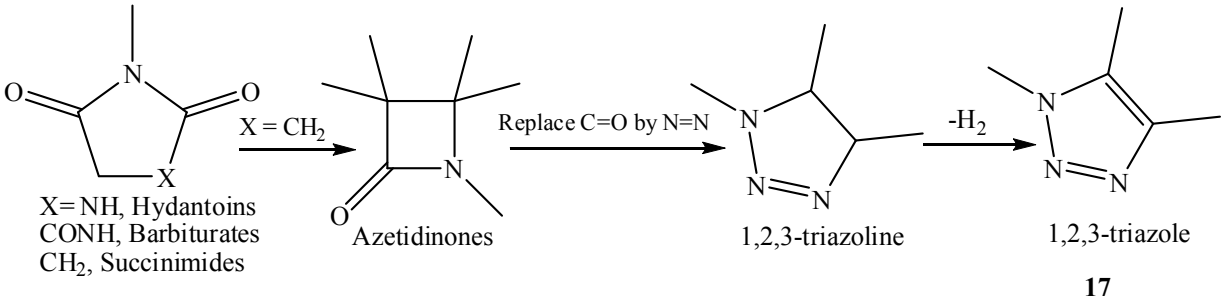
v) Alkylhalide is refluxed with azide in ethanol to furnish 1,2,3-triazole [27][**16**].

vi) 1,2,3-triazoles [**17**] as antiepileptic or anti-convulsantis are formed when dicarboximide entity is absent from the main triazole ring [27].



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Spectral Properties [24-31]

IR Spectral Studies

The IR spectra show (C=N) elongating or stretching at 1600-1650 cm^{-1}, and (C-N) elongating at 1250-1350 $cm^{-1}$and 1261 (N–N=C).

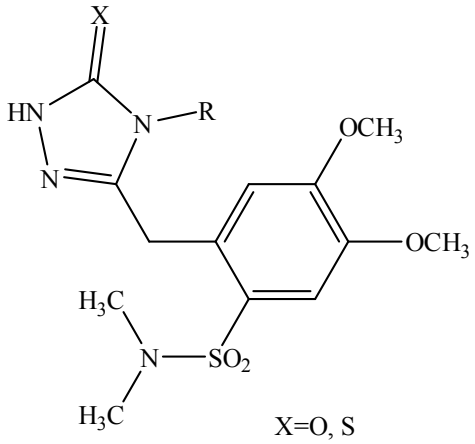
^{1}H NMR Spectra

The ^{1}H NMR spectra of 1,2,4 triazole show two peaks, δ= 13.5, singlet (N-H), δ= 8.27, singlet (2x C-H).

Biological activity of 1,2,4-triazole

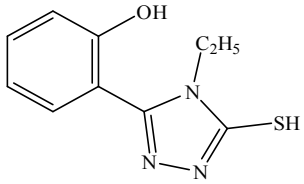
Antibacterial activities

Zoumpoulakis *et al [32]* synthesized a series of derivatives of sulfonamide-1,2,4-triazole which showed promising result of anti-bacterial action comparable with streptomycin and better anti-bacterial effect as compared with chloramphenicol against variety of bacteria. All these compounds exhibited excellent antibacterial potential with MIC in range 0.13–0.65µmol/mL and MBC of 0.24–0.76 µmol/mL. Compound [**18**] showed the most excellent antibacterial action with MIC and MBC of 0.24–0.48 µmol/mL.



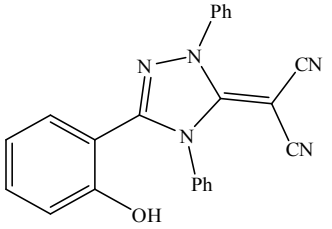
18

Koparir*et al [33]* synthesized 4-ethyl-5-(2-hydroxyphenyl)-2H-1,2,4-triazole-3(4H)-thione. ^{1}H and ^{13}C NMR chemical shift values of III in the ground state was determinedby adopting the density functional method and the DFT calculations was used to obtained the conformational flexibility of the main compound. The synthesized lead compound [**19**] was evaluated for its antibacterial, antifungal and antioxidant potential.



19

Al-Omair *et al [34]* synthesized some new thiadiazoles, tetrazine and triazoles. The characterization of the these compounds was carried out and further, these compounds [**20**] were evaluated for antibacterial potential using four different strains of bacteria like *P. aeruginosa*, *S. aureus, E. coli*, and *B. megaterium*. The antioxidant activities of these synthesized compounds were also carried out by evaluation of DPPH free radical scavenging activity, SOD, NO and ABTS.



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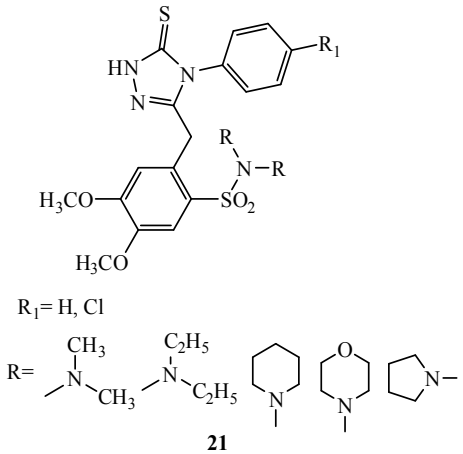
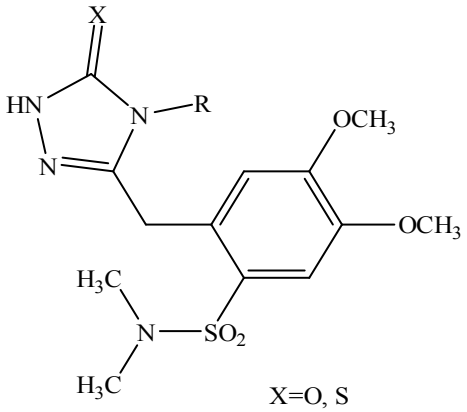
Antifungal activities

Ezabadi *et al [35]* prepared a series of some new 5-[2-(substituted sulfamoyl)-4,5-dimethoxy-benzyl]-4aryl-s-triazole-3-thiones. The screenings of antifungal and antibacterial activities of all these synthesized compounds [**21**] were performed against all the *micromycetes*, using fungicidal bifonazole as standard reference drug.



21

Zoumpoulakis *et al [11]* reported the synthesis of a series of derivatives of sulfonamide-1,2,4-triazole which exhibited promising result of antifungal activity against a series of *micromycetes* using commercial fungicide bifonazole as standard reference. Compound [**22**] exhibited the excellent antifungal activity as compared with rest of the other compounds with least MIC (0.01–0.25 µmol/ml) and MFC (0.03– 0.38 µmol/ml). *Trichoderma viride* was found to be the most sensitive fungi to all compounds under screening, while *Aspergillus versicolor* was found to be the most resistant fungi against tested compounds.

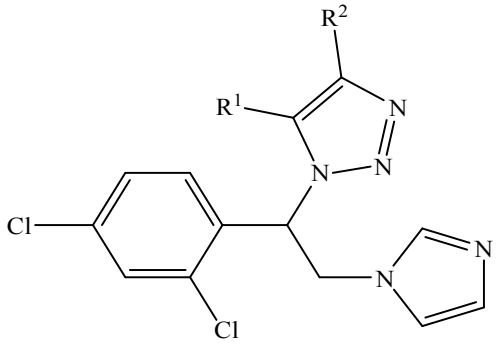


X=O, S

R= $-CH_3$, $-C_2H_5$, $-C_3H_7$, Isopropyl, n-butyl, t-butyl

22

Gonzalez-Calderon *et al [36]* synthesized 1,4,5-tri and 1,5-disubstituted triazole derivatives by azide enolate 1,3-dipolar cycloaddition. All the newly synthesized compounds were evaluated for the antifungal potential. It was observed from these pre-clinical evaluations that compounds [**23, 24**] might be used as lead for further studies.



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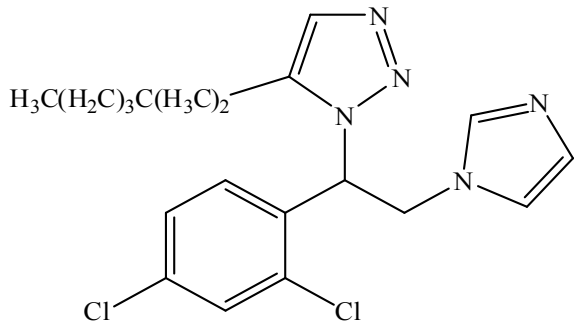

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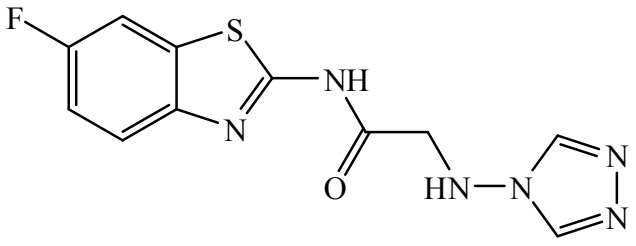
Sidhu *et al [37]* designed and synthesized twenty novel hybrid compounds, 6-flourobenzothiazol-2-yl-1,2,4-triazoles by combining fungicidal leads viz. 6-flouro-1,3-benzothiazol-2-amine and 1,2,4-triazoles in a single molecule. All the synthesized compounds were screened for antifungal activities and it was found that compounds [**25, 26**] have excellent fungal toxicity which was comparable with the standard fungicides used. Structure activity relationship were studied by docking studies and Lipinski filtration.



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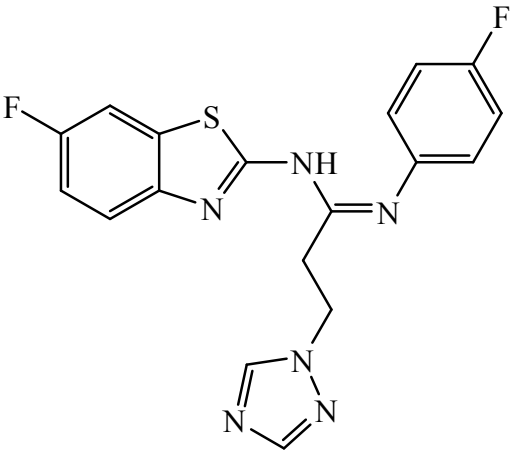
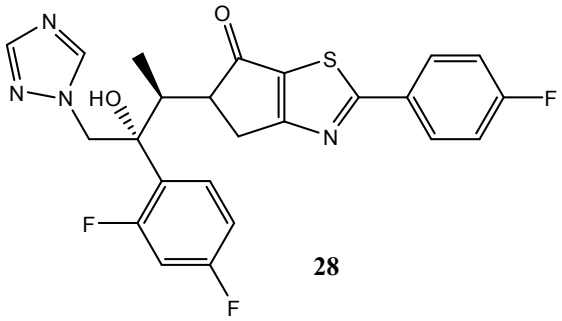


26

Xu *et al [38]* designed, synthesized and characterized some novel triazole derivatives containing ã-lactam ring. The target compounds were screened for their *in vitro* antifungal activities. All these compounds showed stronger anti-fungal activity against the six clinically important fungi tested than fluconazole. Compounds [**27, 28**] showed comparative activity against the fungi tested except for *Candida glabrata* and *Aspergillus fumigatus* as voriconazole.



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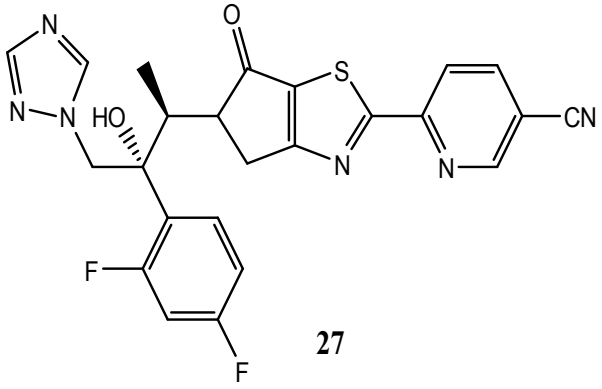
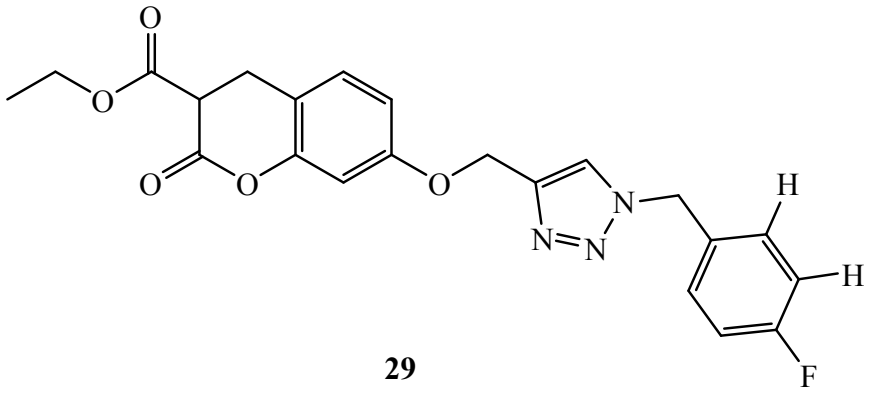


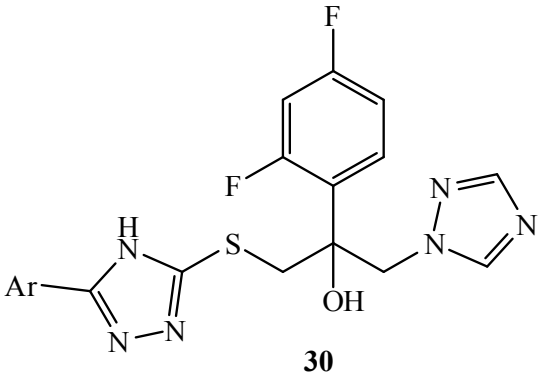
27

Shaikh et al [39] reported potential antifungal activities of a new series of ethyl-7-((1-(benzyl)-1H-1,2,3-triazol-4-yl)methoxy)-2-oxo-2H-chromene-3-carboxylates prepared through click chemistry. All the compounds were screened for the antifungal activity using five fungal strains from human origin. Compound [**29**] was reported to have doubled the antifungal activity in comparison to miconazole and showed equal potency when compared with fluconazole against *C. albicans*. Molecular docking study also performed which showed that the synthesized compound has good binding affinity to active site of fungal *C. albicans* enzyme P450 cytochrome lanosterol 14α-demethylase.



29

Hashemi et al [40] designed and reported two new series of 5-aryl-3-mercapto-1,2,4-triazole derivatives. The synthesized compounds were evaluated for antifungal activity. Among the synthesized compounds, 5-(2,4-dichlorophenyl)-triazole derivatives [**30**] and [**31**] with MIC <0.01 to 0.5 µg/mL were found to be 4–256 times more potent than fluconazole against *Candida* species.



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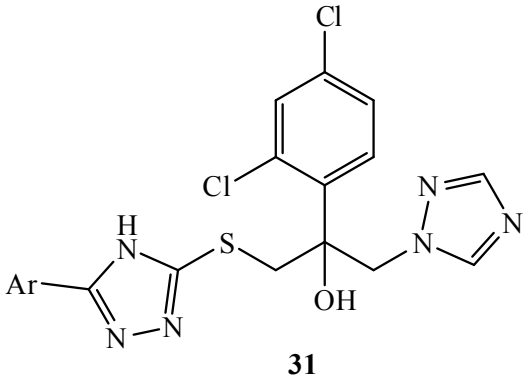
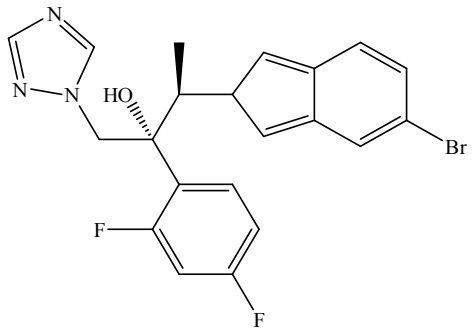


31

Park *et al [41]* reported the synthesis and screening of *in vitro* and *in vivo* antifungal activities of a series of (2R,3R)-2-(2,4-difluorophenyl)-3-(substituted indazol-1-yl)-1-(1H-1,2,4-triazol-1-yl)butan-2-ol derivatives. Compounds [**32**] with 5-bromo substitution on the indazole ring exhibited wonderful activity against *Candida albicans* in a murine model of infection and found to be causing significant improvement in the infected mice for their survival rates.



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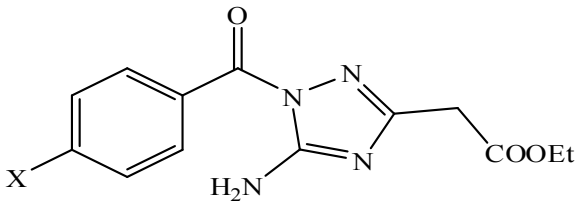
Anti-inflammatory activity

Abdel-Megeed *et al [42]* synthesized a new series of acylated 1,2,4-triazole-3-acetates derivatives. The acute toxicity studies, anti-inflammatory activity and possible gastric ulcerogenic effects of all the synthesized compounds were carried out and reported. The results of anti-inflammatory screening revealed that 1-acylated-5-amino-1,2,4-triazole-3-acetates [**33**] exhibited greater anti-inflammatory effect as compared with their analogous of 5-acylamino derivatives [**34**]using carrageenan-induced model of rat paw edema with little gastric ulcerogenic effects in comparison with indomethacin as standard reference drug.



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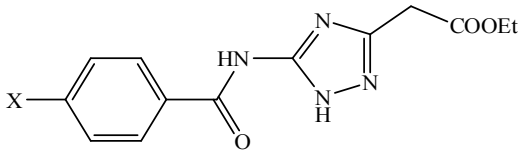
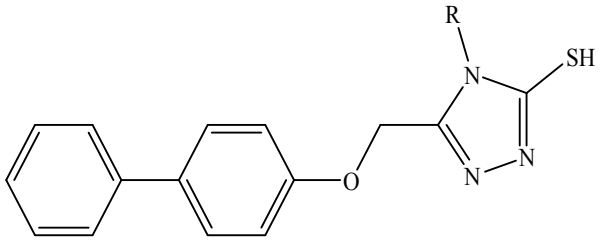


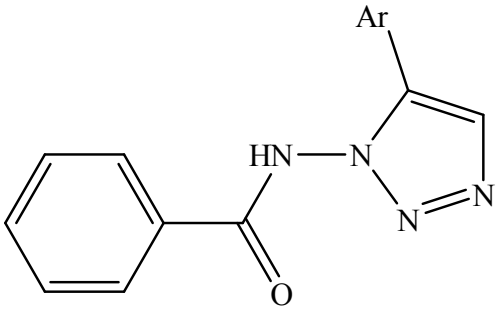
34

Kumar *et al [43]* synthesized a novel series of 1,2,4-triazole derivatives of biphenyl-4-yloxy acetic acid. The carrageenan induced rat paw edema model of inflammation was used to screen all newly synthesized compounds for the anti-inflammatory activity. Compound [**35**] emerged as the lead compound which showed excellent anti-inflammatory action (**81.81**%) as compared with the standard reference drug (**79.54**%), with slight ulcerogenic activity along with excellent protective potential on lipid peroxidation.



35

Murti *et al [46]* reported the synthesis of different 1,2,3- & 1,2,4-triazole derivatives [**36, 37**] derivatives. The Kirby-Bauer disk diffusion method was used for the screening of the antimicrobial activity of these newly synthesized compounds. The anti-inflammatory activity of these compounds was also carried out by using carrageenan-induced model of acute paw edema. The characterization of these compounds was carried out by elemental analysis, ^{1}H-NMR and FT-IR.



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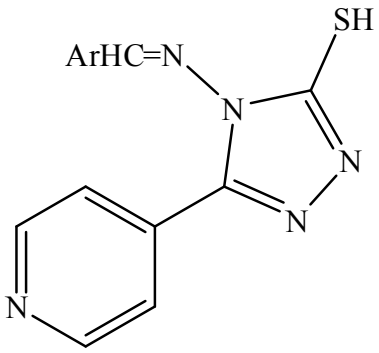
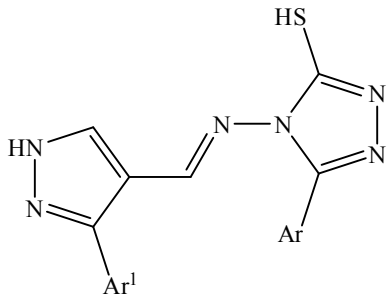


37

Antimicrobial activity

Vijesh et al [44] reported the synthesis of three different series of new benzoxazole and 1,2,4-triazole derivatives having substituted pyrazole moiety. Analgesic activity of all compounds was performed by the tail flick method. These compounds were also screened for their antimicrobial activity by the serial dilution method using Minimum Inhibitory Concentration (MIC).

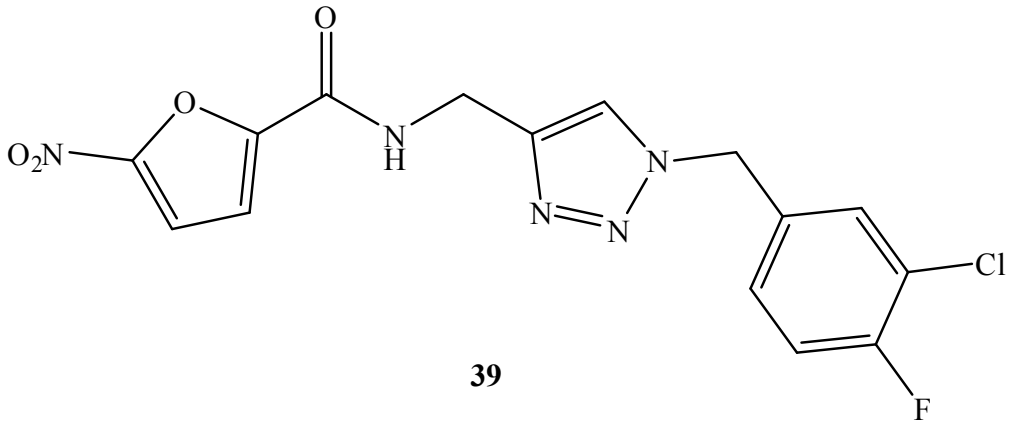
The results of antimicrobial activity showed that the compound [**38**] with 2,5-dichlorothiophene substituent on pyrazole moiety and a triazole ring exhibited excellent antimicrobial and analgesic activity.



Ar1 = 2,4-Dichlorophenyl, 4-Thioanisyl, Biphenyl
2,5-Dichlorothiophene,
Ar = 1-Naphthyloxymethyl, Isonicotinyl, 6-Methylnicotinyl

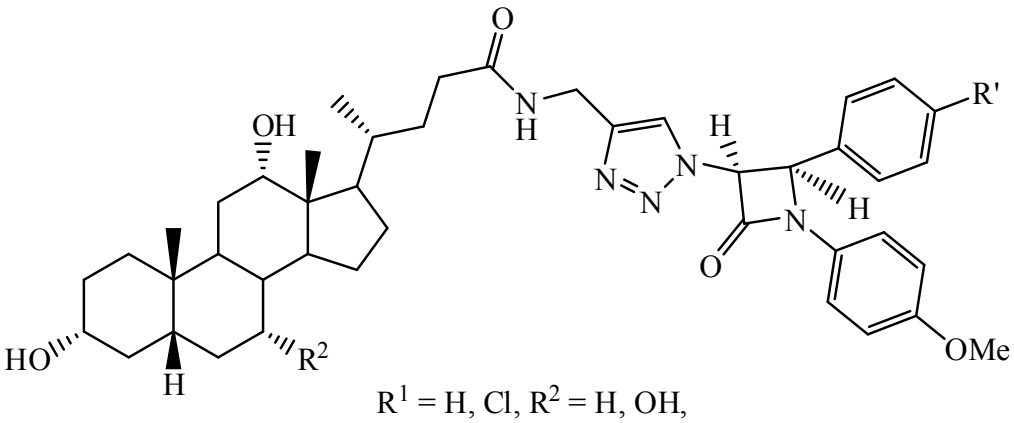
38

Kamal *et al [45]* synthesized a series of 5-nitrofuran–triazole conjugates. All the compounds were screened for their antimicrobial activity against Gram-negative and Gram-positive bacterial strains, and these compounds were also screened for anti-tubercular potential against *Mycobacterium tuberculosis* H37Rv strain. The compound [**39**] showed equal potency as compared with standard reference drug Ciprofloxacin exhibiting MBC value 1.17 µg/ mL against *Bacillus subtilis* bacterial strain. Results also revealed that these compounds found to exhibit excellent anti-tubercular activity having MIC value of 0.25 µg/mL.



39

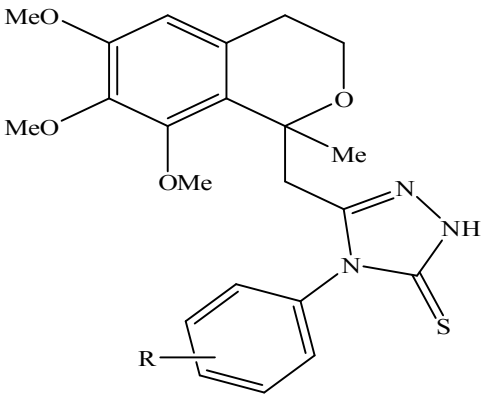
Vatmurge *et al [47]* reported the synthesis of some new 1,2,3-triazole-linked ß-lactam bile acid conjugates using 1,3-dipolar cycloaddition reaction of azido ß-lactam and terminal alkyne of bile acids using Cu (I) as catalyst. Majority of the synthesized compounds [**40**] showed moderate antibacterial activity and excellent antifungal activities against all tested pathogenic strains of bacteria and fungi respectively.



R^1 = H, Cl, R^2 = H, OH,

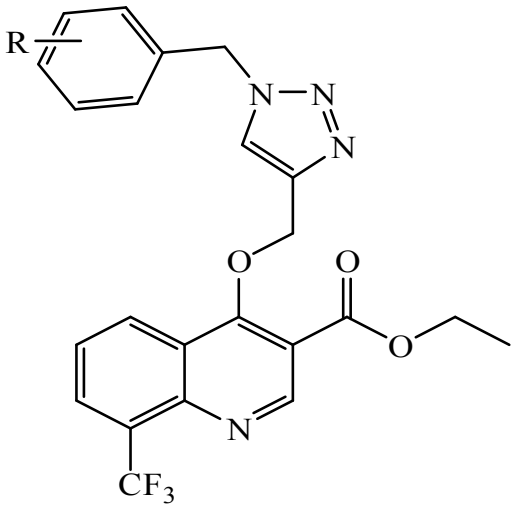
40

Saeed *et al [48]* reported the design and synthesis of new isochroman-triazole and thiadiazole conjugates which were obtained by hetero-cyclization of corresponding isochromanyl thiosemicarbazides. The synthesized new compounds [**41**] were evaluated for *in vitro* antibacterial potential using four bacterial strains and these compounds were found to show good antimicrobial activity toward the tested microorganisms as compared with the standard drug ampicillin.



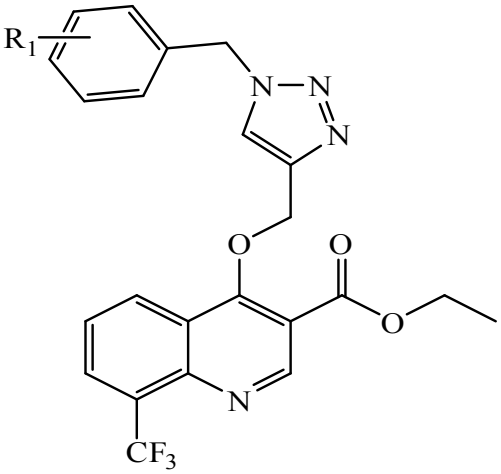
41

Garudachari *et al [49]* synthesized and reported three series of 1,2,3-triazoles derivatives of 8-tri-fluoro-methyl-quinoline by adopting multi-step reactions through click chemistry. The characterization of the synthesized compounds was carried out by X-ray analysis and spectral studies. In-*vitro* antimicrobial activities of the final compounds were carried out by well plate method by measuring zone of inhibition. It was found that compounds [**42, 43, 44**] exhibited excellent antimicrobial potential against tested strains of pathogenic microorganisms.



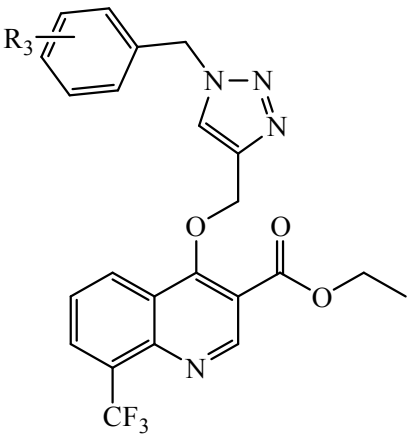
R=H, NO_2, 2,4-Cl

42



R_1= F, Cl, Br, OCH_3;

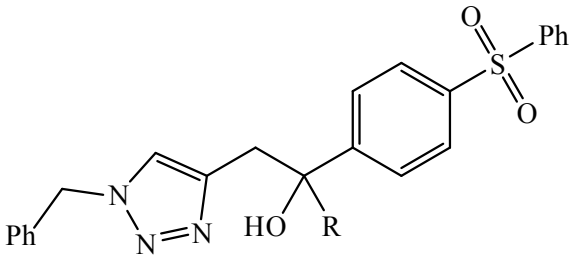
43



R_2=-CH_2CH_3,-$CH_2CH_2CH_3$, -$CH_2CH_2CH_2CH_3$

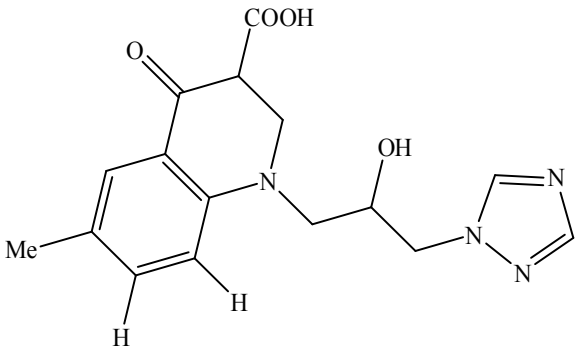
44

Mady *et al [50]* prepared a new series of 1,2,3-triazoles combined with di-aryl-sulfone containing compounds by adopting the copper catalyzed azide-alkyne 1,3-dipolar cyclo-addition reaction under ultra sound irradiation in benign solvents. The antibacterial, antifungal and antioxidant activities were carried out for all newly synthesized compounds. The DPPH free radical scavenging assay was used to screen the antioxidant activity of all synthesized compounds. It was found that compound [**45**] possess an excellent antioxidant activity.



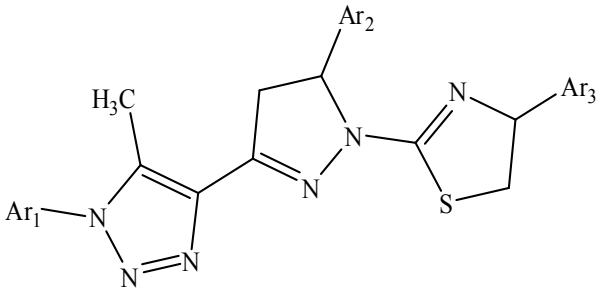
45

Cui *et al [51]* synthesized and evaluated a new series of quinolone triazoles derivatives. Antimicrobial activities of these compounds were evaluated against four fungi and seven bacteria including multi-drug resistant MRSA using Fluconazole as standard antifungal, while Norfloxacin and Chloromycin as standard antibacterial reference drugs. The compound [**46**] evaluated for preliminary interactive studies and observed that it might efficiently interact with DNA and formed compound 46-DNA complex. This compound-DNA complex could block DNA replication, hence produced its antimicrobial effects.



46

Abdel-Wahab *et al [52]*synthesized and characterized some novel pyrazolyl-1,2,3-triazoles and 1,2,3-triazol-4-yl-pyrazolylthiazoles by multistep reactions. The characterization of newly synthesized compounds was carried out by elemental and spectral analyses. The antimicrobial activities of synthesized compound [**47**] against test microorganisms showed very good antimicrobial activity amongst all the compounds.

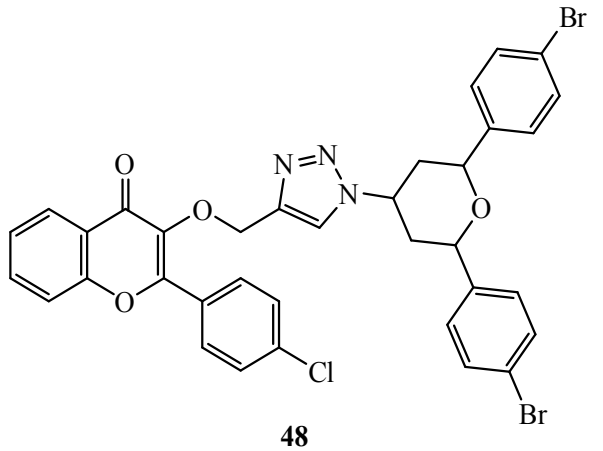


Ar_1= 4-MeC_6H_4; Ar_2= 4-FC_6H_4
Ar_3 = Ph, 4-ClC_6H_4, 4-BrC_6H_4

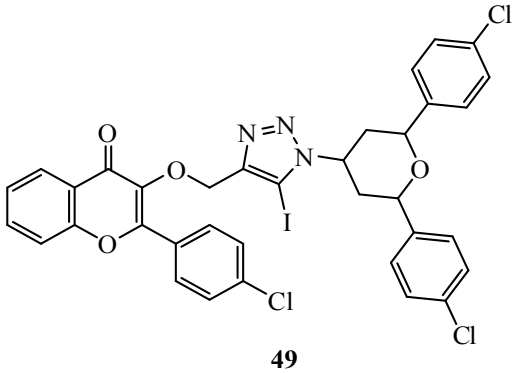
47

Anticancer activity

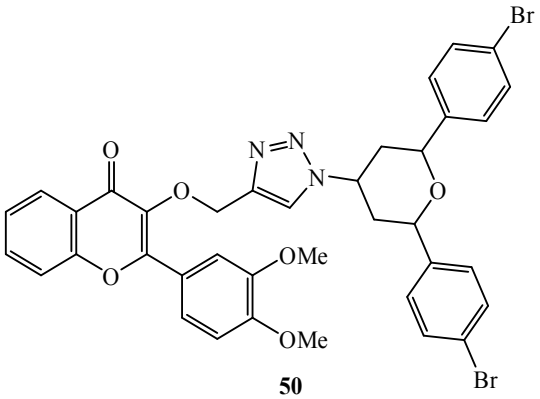
Ahmed *et* al [53] synthesized new derivatives of 1,4-disubstituted 1,2,3-triazoles. The anti-proliferative activity of all newly synthesized compounds were carried out using three different types of human cancer cell lines (MDA-MB 231, KCL22 and HeLa. The compound [**48**] with IC_{50} 0.70 µM, compound [**49**] with IC_{50} 0.61 µM and compound [**50**] with IC_{50} 0.65 µM showed better anti-proliferative activity as compared with the reference drugs using MDA-MB 231 cell lines, KCL22 cell lines and HeLa cell lines, respectively.



48

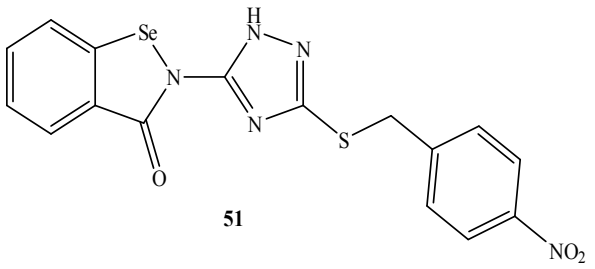


49



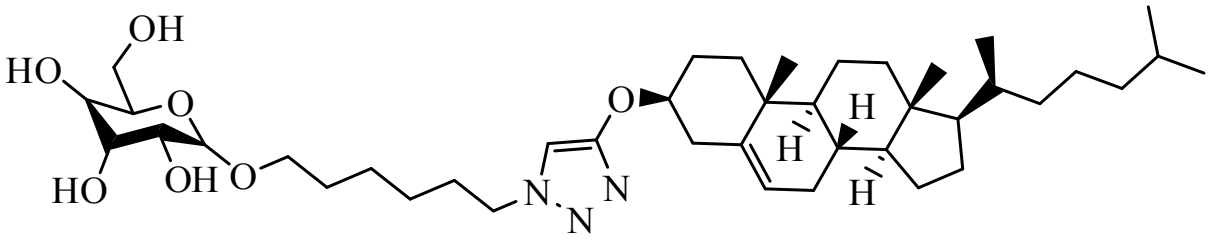
50

Li *et al [54]* reported the design and synthesis of a new series of 1,2,4-triazole derivatives integrating benziso-selenazolone scaffold. The *in vitro* antiproliferative activities of all newly synthesized compounds were screened against human cancer cell lines SMMC-7721, HeLa, A549, and normal cell lines L929 by CCK-8 assay. The Compound [**51**] found to have excellent antiproliferative action against HeLa cells and the strong inhibition against A549 cells with IC_{50} value 3.94 μM and 9.14 μM, respectively.



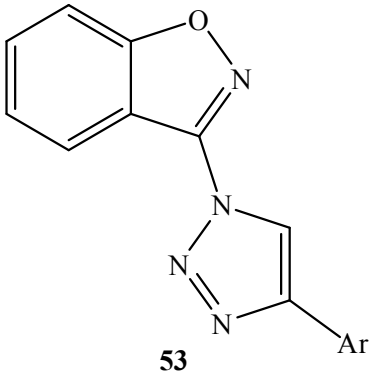
51

El Sayed Aly *et al [55]* prepared a series of triazole derivatives by CuAACof two azido substrates. The *in vitro* antimicrobial activity and cytotoxic potential of these compounds were carried out. Compound [**52**] was found to be most active among all synthesized compounds.



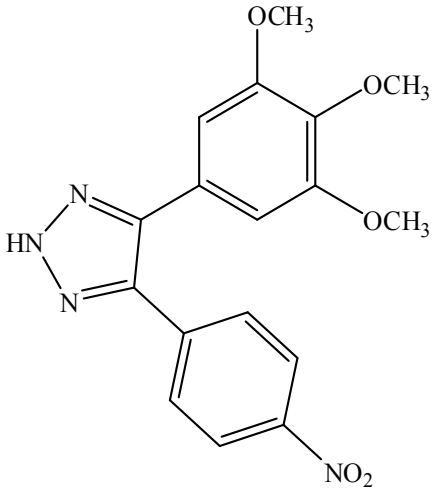
52

Ashwini et al [56] prepared several 1,2,3-triazole-based heterocycles which showed excellent anticancer activity in a variety of tumor models. The title compounds 3-(4-(4-phenoxyphenyl)-1H-1,2,3-triazol-1-yl)benzo[d]isoxazole (PTB) were evaluated with excellent antiproliferative activity against human acute myeloidleukemia cells. In MTT assay of all tested compounds [**53**] the title compound emerged as the most powerful and potent antiproliferative agent with an IC_{50} of 2 μM against MV4-11 cells.

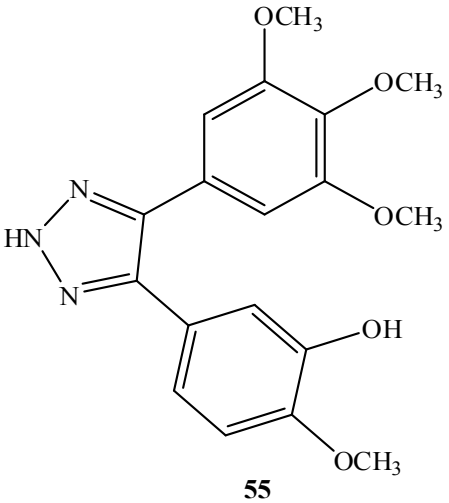


53

Madadi *et al* [57] synthesized a series of analogues of combretastatin A-4 (CA-4). tHESE analogues were synthesized from (Z)-substituted diarylacrylonitriles. In the screening studies for anti-cancer activity, the di-aryl-acrylonitrile analogue [**54**] emerged as the most potent compound having GI_{50} values of <10 nM against nearly all the human cancer cell. In in-silico docking studies, compound [**55**] emerged as lead compound with better affinity for the colchicine binding site of tubulin in comparison to the compounds [**54**].

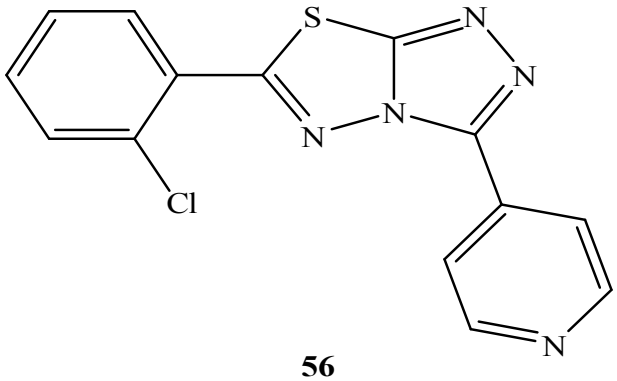


54



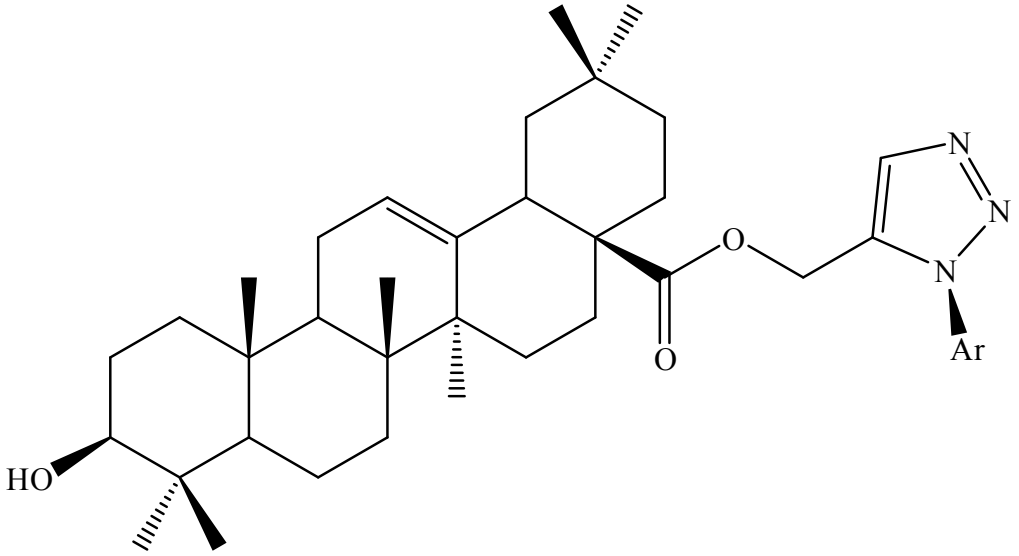
55

Kamel and abdo, 2014 [58] synthesized a new series of triazolo[1,3,4]thiadiazoles derivatives. The compounds were screened for *in vitro* anticancer activity and found that the compound [**56**] showed equal cytotoxic potential as compared with the standard CHS 828 using gastric cancer cell line (IC_{50} = 25 nM).



56

Chouaý *et al [59]* quantitatively isolated a natural pentacyclictriterpenoid "**the oleanolic acid**" from pomace olive (*Olea europaea L*) and then synthesized two series of oleanolic acid. The structure elucidation of the synthesized compounds was performed with ^{13}C NMR, ^{1}H NMR, HRMS and NOESY analyses. The biological screening results revealed that Oleanolic acid possess excellent anticancer action against human colon (SW480) and murine breast (EMT-6) cancer cells. The derivatives of Oleanolic acid [**57**] (1,5-regioisomer) also exhibited excellent anti-cancer potential.

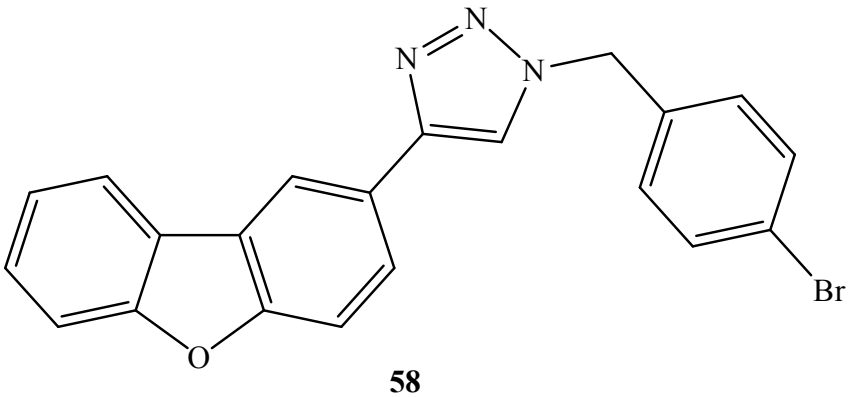


Ar = -C_6H_5, 4(MeO)C_6H_4, 4(Cl)C_6H_4, 4(Br)C_6H_4, 4(NO_2)C_6H_4, 4(me)C_6H_4, naphthyl

57

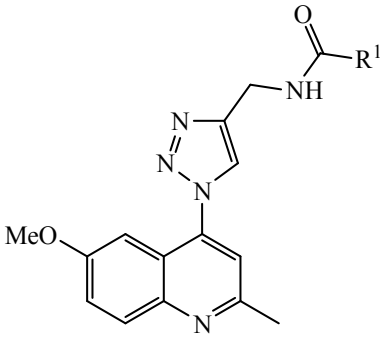
Antitubercular activity

Yempala *et al [60]* synthesized a new series of dibenzo[b,d]furan-1,2,3-triazolesderivatives. *In vitro* antimycobacterial activity of all the synthesized compounds against *Mycobacterium tuberculosis* was carried out. Compound [**58**] showed the best anti-tubercular agent having minimum cyto-toxicity (selectivity index: ÃÃ25) against the HEK-293T cell line among these three compounds.



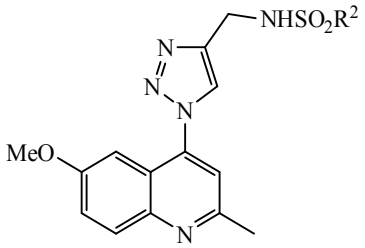
58

Thomas *et* al [61] reported the synthesis of three new series of quinoline-4-yl-1,2,3-triazoles having sulphonamides, amides, and amido-piperazines. The characterization of all the newly synthesized compounds was done by elemental and spectral analysis. The anti-tubercular activities of all the compounds were evaluated against *Mycobacterium tuberculosis* H37Rv strain. Compounds, [**59, 60, 61**] showed excellent anti-tubercular activity against *Mycobacterium tuberculosis* H37Rv strain.



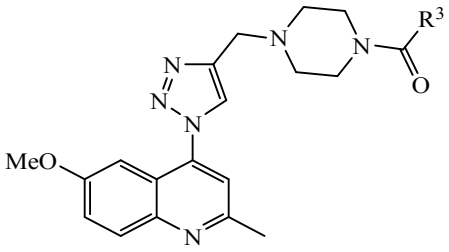
R^1= Acetyl, 4-Fluoro benzoyl, 4-Methoxy benzoyl, 4-Trifluoro methylbenzoyl

59



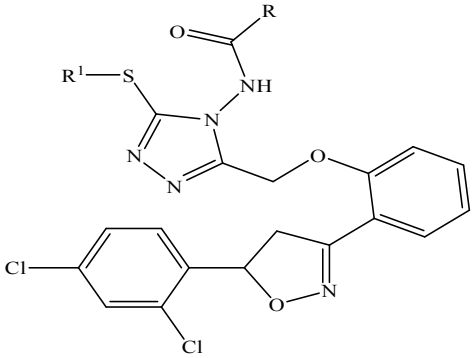
R^2= 4-Methoxy benzene

60



R^3= 4-Methoxy benzoyl, Benzoyl

61



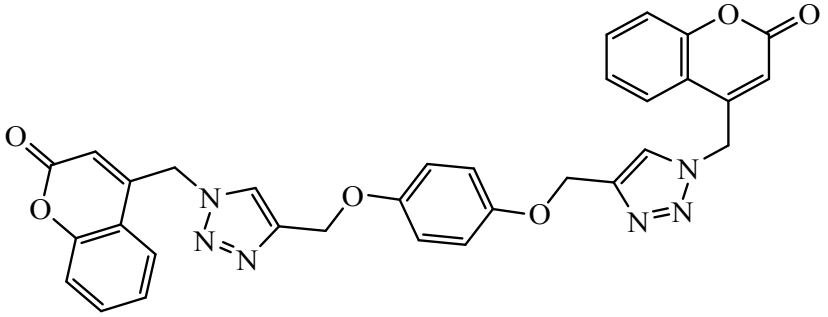
R=-CH_3, -C_6H_5, $COCH_2Cl$, R^1=-C_2H_5, -C_3H_7

62

Dixit *et al [62]* reported the synthesis of hybrid compounds by coupling known efflux inhibitors (EI) and triazole. This synthesis was aimed to identify pharmacophore from known efflux inhibitors.

The synthesized compounds were screened as Efflux inhibitor and growth inhibitors of tuberculosis initially against *Mycobacterium smegmatis* (2)155. Compound **[62]** emerged as the most powerful and potent dual inhibitor of tuberculosis among all compounds.

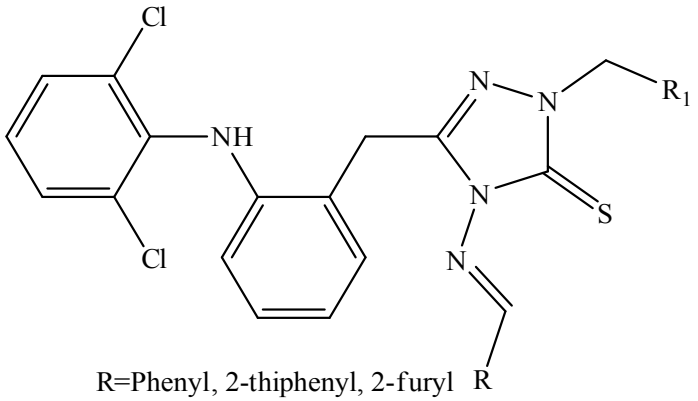
Anand *et al [63]* synthesized a new series of hybrids of bis-triazole coumarin derivatives using aryl propargyl ethers and 4-(azidomethyl)-2H-chromen-2-ones by Click chemistry. All the compounds were screened for anti-tubercular. These results were further evidenced by molecular modeling and 3D-QSAR studies by means of CoMFA and Topomer CoMFA. Finally, it was found that the bis-triazole compound **[63]** exhibited excellent antitubercular activity.



R= 6-CH_3, 7-CH_3, 5,7-Di CH_3, 7,8-Di CH_3, 7-OCH_3, 7,8-Benzo

63

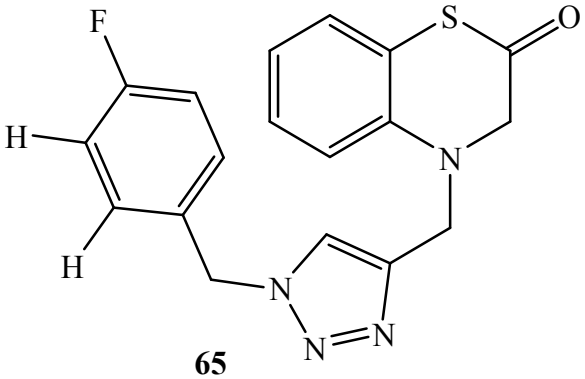
Krishna *et al [64]* designed and synthesized a new series of diphenylamine containing 1,2,4-triazoles. The in-vitro anti-mycobacterial and anti-bacterial activities of all newly synthesized compounds was evaluated. Out of all, compound [**64**] have shown potential activity against *Mycobacterium tuberculosis* H37Rv strain with MIC of 0.2, 1.6 and 3.125 μM, respectively. All the compounds were studied for SAR and it was found that diphenylamine containing 1,2,4-triazoles are strong anti-mycobacterial agents.



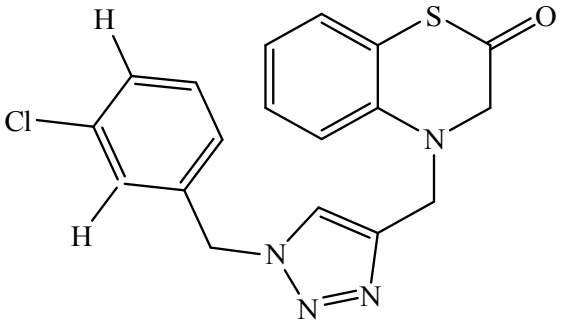
R=Phenyl, 2-thiphenyl, 2-furyl

64

Shaikh *et al [65]* synthesized benzothiazinone based 1,2,3-triazoles derivatives by click chemistry way of approach for the search of new antitubercular agent. These newly synthesized compounds were subjected for anti-proliferative activity and antitubercular activities. Among all the synthesized compounds,[**65**] and [**66**] were the most active compound against *MTB* and *M. bovis* BCG. These synthesized compounds were also found to have potential antioxidant activity. The molecular docking studies of these compounds also supported the significant biological activity.

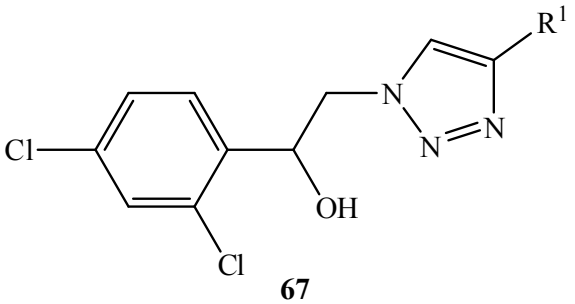


65



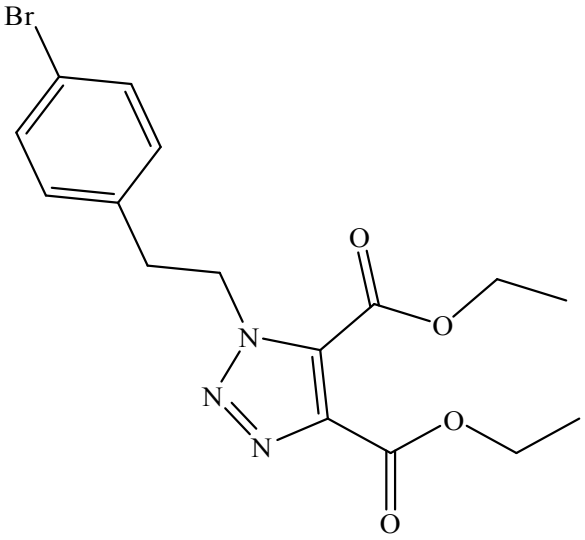
66

Kim *et al [66]* reported the synthesis of 1H-1,2,3-triazoles, synthesized from econazole as starting material by microwave-assisted click chemistry. Majority of the Hydroxy-triazoles exhibited antitubercular activities against *Mycobacterium tuberculosis*. The MIC of the hydroxy-triazole was comparable with the econazole (16 μg/mL) and the MIC of [**67**] was found two times more active in comparison with econazole. It was concluded that hydroxy-triazoles were found to have more activity as compared with their corresponding ether-triazoles.



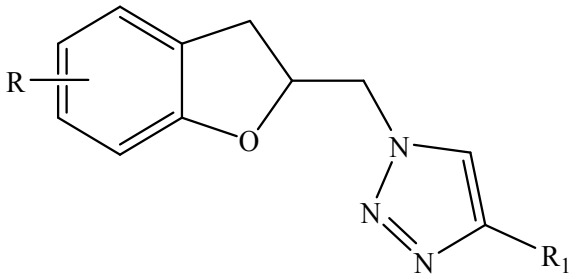
67

Shanmugavelan *et al [67]* synthesized some new derivatives of 1,2,3-triazoles. These derivatives were obtained only in 1-3 minutes in solvent-free conditions. Anti-tubercular activity of these triazole compounds were evaluated against *Mycobacterium tuberculosis* H(37)Rv strain and found that four compound [**67**] exhibited potential anti-tubercular activity with MIC in the range from 1.56 to 3.13 μg/mL.



67

Tripathi *et al [68]* synthesized 1,4-disubstituted-1,2,3-triazoles derivatives by [3+2] cyclo-addition of different alkynes with various types of 2-(azidomethyl)-dihydronaptho (benzo) furans. All the newly synthesized compounds were evaluated against *Mycobacterium tuberculosis* H37Rv for their antitubercular activities. It was observed that compound [**68**] was found to possess excellent antimycobacterial activities with MIC from 12.5-3.12 μg/ml.



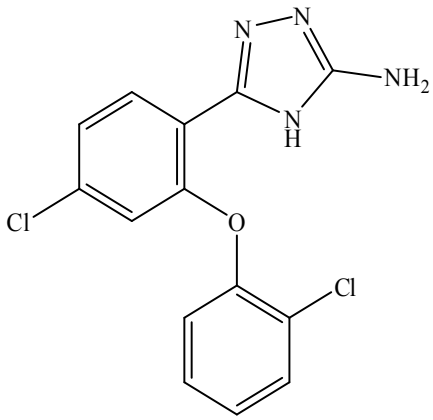
R=-4-CHO, -2,5-Di-Me

R_1=$-(CH_2)_4CH_3$, $-(CH_2)_5CH_3$, –CH2OH

68

Anticonvulsant activity

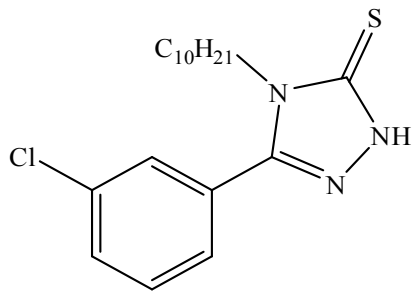
Ayati *et al [69]* designed and synthesized some triazole derivatives [**68**] as anticonvulsant or antiepileptic agents. Triazoles containing heterocyclic compounds are important class of drugs and might be useful for the synthesis of new molecule as anticonvulsant drugs.



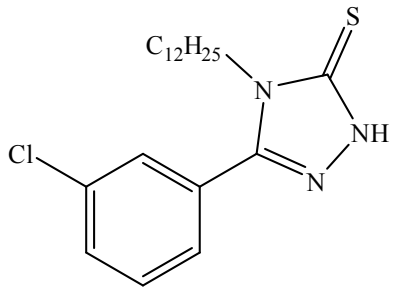
68

Plech *et al [70]* reported the design and synthesis of 4-alkyl-1,2,4-triazole-3-thione derivatives. These compounds were evaluated for their anticonvulsant activity against maximal electro-shock-induced seizure model of animals. A selective and sensitive method based on HPLC inbuilt with diode array detector was also used for the estimation of the level of anticonvulsant compounds in the brain tissues of the mice. Further, chromatographic analysis was also done and it was found that two derivatives [**69, 70**] with long alkyl chains at N-4 position of the 1,2,4-triazole ring did not produce any anticonvulsant

effect since these compounds were not capable to cross the blood-brain barrier.

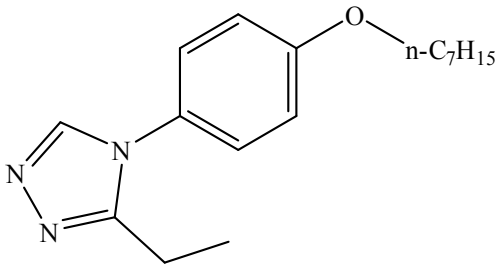


69



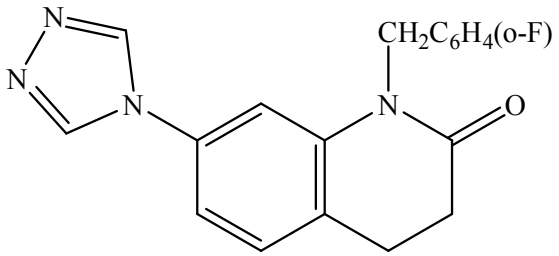
70

Chen *et al [71]* reported the synthesis of new series of 4-(4-alkoxylphenyl)-3-ethyl-4H-1,2,4-triazole derivatives The synthesized compounds were evaluated for their anticonvulsant potential using the maximal electro-shock test animal model of seizures (MES test) and the neurotoxicity. The results of the MES test demonstrated that compound [**71**] is most potent compound (ED_{50}=8.3mg/kg) and protective index ($PI=TD_{50}/ED_{50}$ equal to 5.5).



71

Deng *et al [72]* prepared a series of 1-substituted-6-(4*H*-1,2,4-triazol-4-yl)-3,4-dihydroquinolin-2(1*H*)-ones derivatives. The newly synthesized compounds were evaluated for their anticonvulsant and antidepressant potentials. Besides this, compound [**72**] demonstrated better efficacy as compared with fluoxetine in the tail suspension test. These results were further confirmed by an open field test, and compound [**72**] showed excellent antidepressant activity.



72

Conclusion

Triazole derivatives show wide range of therapeutic and pharmacological actions. The present review compiles the synthesis, design and potential biological activities of several new triazole derivatives. Some of these newly synthesized compounds could be used in near future as lead compound for preparing potential drug candidate. Triazole derivatives may be used for the development of newer antibacterial, antifungal, anti-inflammatory, analgesic, antimicrobial, anticancer, antitubercular, and anticonvulsant agents. It is conceivable that with proper designing, synthesis, structure activity relationship, and screening, highly potent and safer biologically active triazoles could be developed.

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