Review Article

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Pharmacological activities of Triazole analogues as antibacterial, antifungal, antiviral agents

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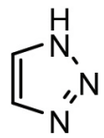
Abstract

Triazoles and its derivatives possess a great importance in medicinal chemistry and can be used for the synthesis of various compounds with different types of biological activities. The triazole derivatives are possessing divers biological activities such as antibacterial, antifungal, antiviral, antitubercular, anti-inflammatory, analgesic, antitumor, anticonvulsant and some other biological as well as chemical useful compounds. The biological profile of triazole moiety has attracted the attention of many researchers to explore its multiple potential against several biological activities. This article covers the information of some triazoles derivatives having antimicrobial activities. Thus triazole acts as a promising medicinal agent and can be helpful to develop new triazole compounds that could have better efficacy and lesser toxicity.

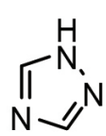
Keyword: Triazole compounds, antibacterial, antifungal, antiviral

1. INTRODUCTION

Triazole derivatives possess a large significance in medicinal chemistry and numerous heterocyclic triazole compounds having different biological activities. Triazole is a five membered basic compound, containing two carbon and three nitrogen atoms having molecular formula $C_2H_3N_3$. It forms a pair of isomeris[1-6]. The 1,2,3-triazole is measured to be the most stable compound in relationship to all other compounds possessing three adjacent nitrogen atoms. Triazole derivatives possess wide variety of pharmacological activities such as antifungal, antibacterial, antiviral, anticancer, anticonvulsant, anti-inflammatory, antioxidant, anti-tubercular, anti-malarial, anti-nociceptive and other anti-cipated activities[7-15].



1,2,3-triazole



1,2,4-triazole

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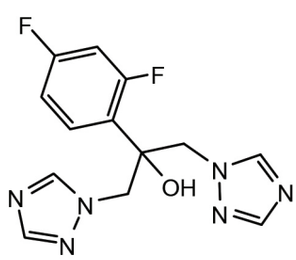
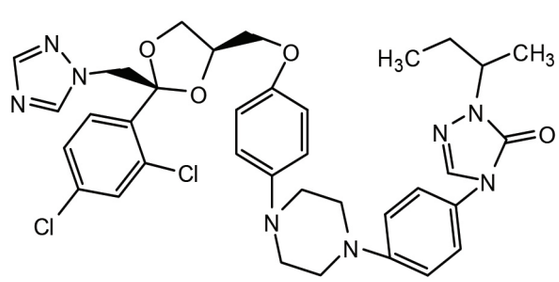
Triazole is measured to be the most useful constituent and widely used in research purposes as a building block for complex chemical compounds and drug molecules such as antifungal drugs fluconazole, isavuconazole, itraconazole, voriconazole, pramiconazole, and posaconazole. The triazole produced plant protection fungicides like epoxiconazole, triadimenol, propiconazole, metconazole, cyproconazole, tebuconazole, flusilazole paclobutrazol and tazobactam. Various substituted triazole compounds are responsible for producing antibacterial effects and further modifications can be made on it to enhance their antimicrobial effects[16-22].



Fluconazole



Itraconazole

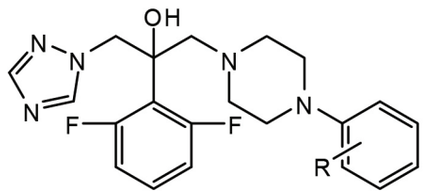
2. ANTIMICROBIAL ACTIVITIES

Bacteria are the simplest and smallest unicellular organism originate independently or in bunches. The huge number of extremely effective and comparatively non-toxic drugs available for the management of bacterial infections has provided tough contest for the medicinal chemist, challenging to synthesis of new antimicrobial agents. These antibacterial agents are classified in two types on the basis of their mode of action as bactericidal and bacteriostatic activities[23-30].

Antimicrobial and antifungal activity: The 1-(1H-1,2,4-triazolyl)-2-(2,4-diflurophenyl)-3-(4-substituted-1-piperazinyl)-2-propanol derivatives on the basis of the active site of lanosterol 14α-demethylase exhibited i*n vitro* antifungal activities. Some of these compounds had higher antifungal activity than fluconazole and some compounds showed good MIC values less than 0.125µg/mL and more potent than fluconazole. Compound **1** and **2** had excellent effectiveness against a broad range of pathogenic fungal stains including *Aspergillus fumigates*[31]. Some ciprofloxacin analogues (**3**) showed antimicrobial activity. In these compounds ciprofloxacin have been incorporated to the series of Schiff bases of 1,2,4-triazole via Mannich reaction. The compounds showed in vitro antimicrobial activity against gram positive and gram negative bacteria like *B. subtilis, K. pneumoniae,* and *P. aeruginosa* at 10µg/mL concentration. All the compounds showed comparable or superior activity than the reference drug ciprofloxacin[32]. Unsubstituted and 3-substituted-7-aryl-5*H*-6,7-dihydroimidazo [2,1-*c*][1,2,4]triazoles (**4**) were exhibited their antifungal activity against *A. niger* and *Fusarium oxysporum.* Among these compounds, 7-(3-chlorophenyl)-6,7-dihydro-5*H*imidazo[2,1-*c*] [1,2,4]triazole-3-thiol was showed the most significant activity[33]. Compounds (**5** and **6**) were evaluated as antimicrobial agents against against *Esherichia coli*, *P. auroginosa*, *Yersinia pseudotuberculosis*, *Klepsiella pneumonia*, *Enterococcus fecalis*, *Staphylococcus aureus* and *Bacillus cereus* and ampicillin was used as control antibiotics. These compounds were showed good antibacterial activity against *S. aureus*[34]. The 1,2,4-triazole-3-thiol metronidazole derivatives (**7a-c** and **8a-c**) were showed anti microbial agents against G-positive, G-negative bacteria and fungal. With the exception of *Clostridium sporogenes* the antimicrobial activity was significantly lower than that of the reference antimicrobials[35]. A series of Schiff bases of triazoles showed antibacterial as well as antifungal activity like 5-phenyl,4-(substituted)amino,3-mercapto-1,2,4-triazoles (**9**) showed antimicrobial activity[36]. Schiff's bases N-[1-arylmethelene]-1-[8-(triafluromethyl) quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carbohydrazide and 1-aryl-4-{1-[8-(triafluro methyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-yl}prop-2-en-1-one containing triazole and quinoline moiety (**10**) were showed their antimicrobial activities against *E. coli*, *S. aureus*, *P. aeruginosa, B. subtilis*, *Klebsiella pneumonia, Aspergilus flavus, A. fumigates, Candida albicans, Penicillium marneffei, Trichophyton mentagrophytes*[37].

A series of N,N-bis(1,2,4-triazole-1-yl methyl) amine (**11,12,13**), condensation of 1-(hydroxyl-methyl) with different amines were evaluated for their antifungal activity against budding yeast *Saccharomycces cerevisiae* and their antibacterial activity was found most active[38]. Antimicrobial activity of some compounds (**14, 15, 16**), 1-(5-phenylamino-[1,3,4] thiadiazole-2-yl)methyl-5-oxo-[1,2,4]triazole and 1-(4-phenyl-5-thioxo-[1,2,4]triazol-3-yl)methyl-5-oxo-[1,2,4] triazole derivatives were found to be potent against various microbes[39]. Several 3,6-Disubstituted-1,2,4-triazolo [3,4-b]-1,3,4-Thiadiazole and their dihydro analogues (**17a-e**) were exhibited their antibacterial, antifungal, anti-inflammatory and analgesic activities. The antimicrobial results showed that some of the compounds are active against both G-positive and G-negative bacteria. These compounds also showed good inhibition of growth of the yeast-like *C. albicans* and fungi *A. niger*[40]. Some 4-Aryl triazole derivative (**17**) were found as antibacterial agents against *B. cereus*, *P. aeriginosa*, *K. pneumoniae, Micrococcus flavus* and *Citrobactor freundii* and antifungal agents against *Candida tropicalis, C. albicans, Cryptococcus neofomans, Trichospor onbeigelii,* and *A. flavus*[41]. The 3-(substituted phenoxymethy)-6-phenyl/substituted phenoxymethyl-1,2,4-triazolo(3,4-B)-thiadiazole

derivatives (**18** and **19**) were showed their in-vitro equipotent antibacterial and antifungal activity at MIC of 1µ g/mL when compared with standard drug respectively. These compounds were showed comparable antitubercular activity against *M. tuberculosis* at MIC of 0.50µg/mL, when compared with standard drug Rifampin and Isoniazid at MIC of 0.25µg/mL[42]. A series of N-(6-bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-2-(4-(3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl)-5-(pyridin-4-yl)-5-thio)acetamido-1,2,4-triazoles (**20a-f**) were showed their antibacterial activity against *S. aureus, E.coli, P. vulgaris, K. pneumonia*[43].



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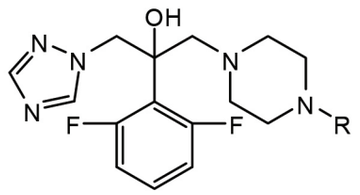

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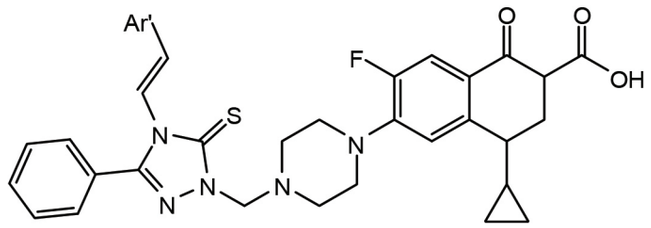

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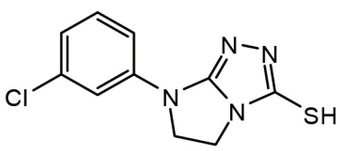

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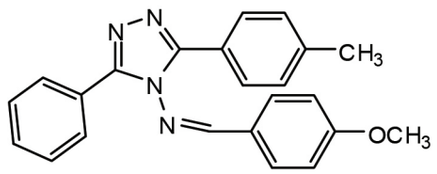

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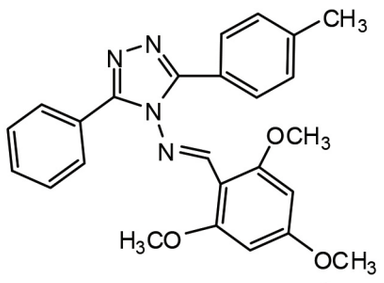

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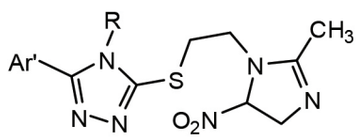
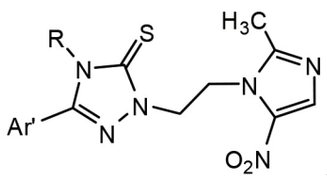


7a -e



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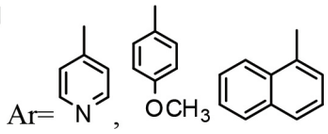

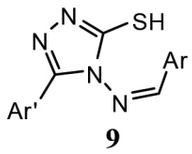

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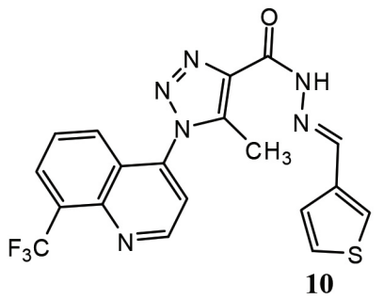

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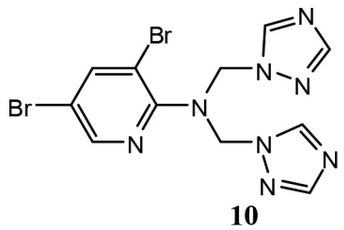

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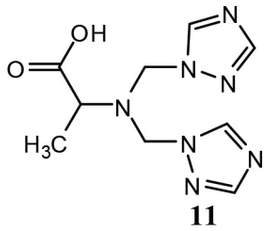

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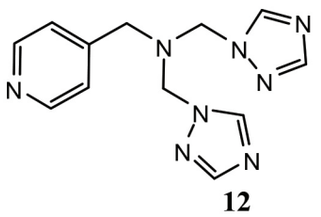

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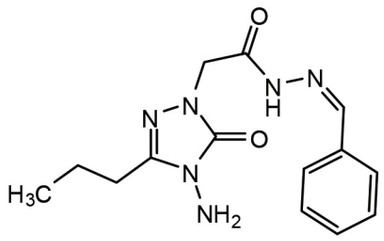

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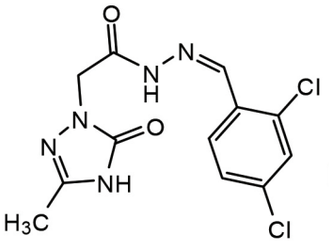

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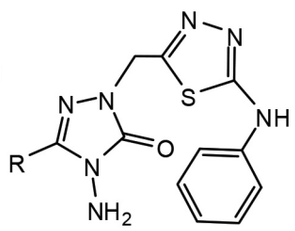
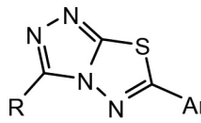
15a-c

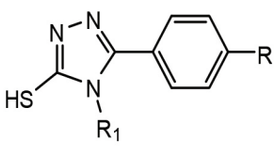


R:a=CH_3,b=$CH_2C_6H_5$,c=C_6H_5

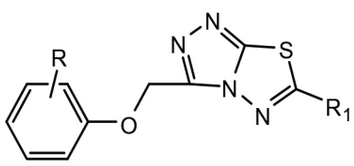


17a-c

R= 2-Chloromethoxy phenyl, 3,4-Dimethoxy benzyl, 2-Methyl-3-Furanyl; Ar'=2-phenyl-4-quinolinyl, 2-methyl-4-quinolinyl, 4-Quinolinyl, 6-Dihydroxy-4-piperydinyl, 5-methoxy-3-indolyl methyl



18 R= -OC_2H_5



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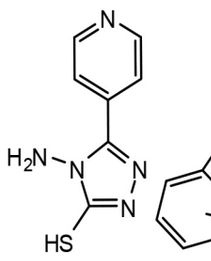
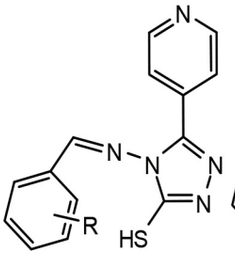


20a



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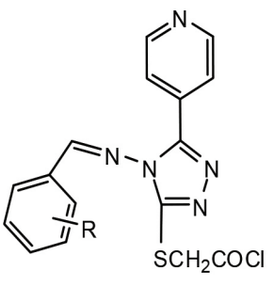

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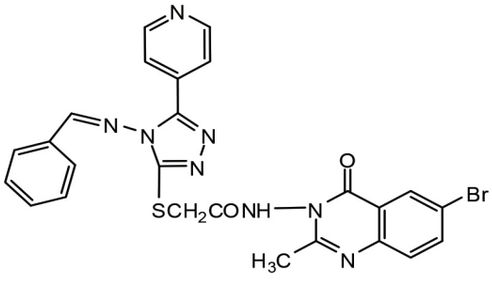

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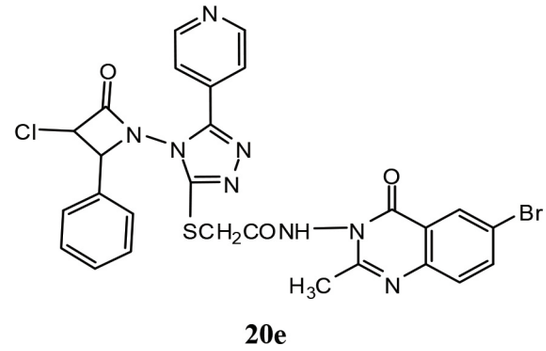
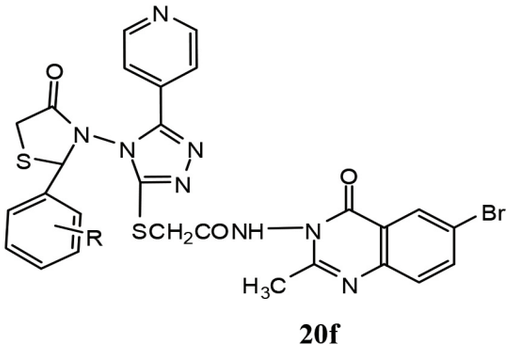


20e

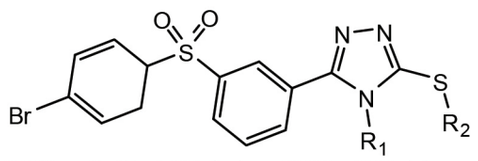


20f

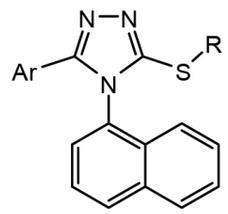
Figure 1. Structure of some triazole compounds with antimicrobial activities

The 1,2,4 -triazole derivatives have good antibacterial activity, S-alkylated-1,2,4-triazoles (**21**) incorporating diphenyl sulphone moieties possess potential antibacterial activity. The pyridyl and naphthyl substituted 1,2,4-triazole (**22**) was showed antibacterial activity[44]. Some 1,2,4-triazole derivatives (**23, 24**) had shown inhibitory activity against some bacteria[45,46].

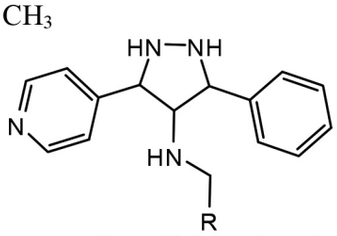
Some 1,2,4-triazole derivatives (**25**) were showed antibacterial activity[47]. The 2,4-dihydro-1,2,4-triazol-3-one derivatives (**26**) were also showed antibacterial activity[48]. The 4-(5-nitro-2-furfurylidene) amino-3-mercapto-5-(substituted)-1,2,4-triazoles (**27**)[49] and some 1,2,4-triazoles (**28**) were exhibited antibacterial activity[50]. Antifungal activity of some 1,2,4-triazole has been shown, the 4-substituted-5-aryl-1,2,4-triazoles (**29**)[51] and 1,2,4-triazolium derivatives (**30**) were exhibited antifungal activity[52]. Some novel mannich bases derived from 3-(4,6-disubstituted-2-thiomethyl-pyrimidyl)-4-amino-5-mercapto-1,2,4-triazoles (**31**)[53] and 1,2,4-triazole derivatives (**32**) were revealed antifungal activity[54].



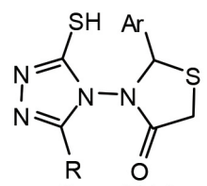
21 R_1 -C_6H_4-CH_3(m) , -C_6H_4-CH_3(p); R_2 -C_2H_5, -C6H4COCH3, CH_3COOCH_3 CH_3



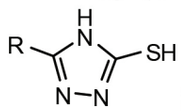
22 Ar= 2-Pyridyl, 3-Pyridyl, 4-Pyridyl R=-CH_2-C_6H_5, -



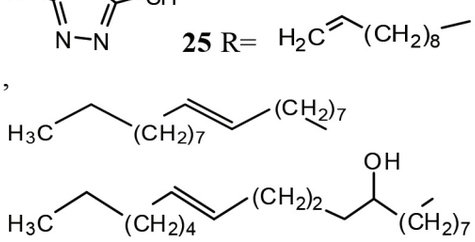
23 R= -C_6H_4Cl (p), -$C_6H_4OCH_3$(p),-$C_6H_2(OCH_3)_3$

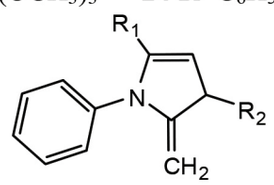


24 R -C_6H_5, -C_6H_4Cl(p) , -$C_6H_4OCH_3$(p)

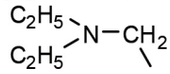


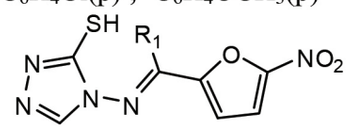
25 R=



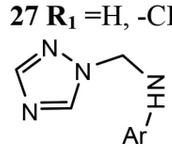


26 R1=H; R_1 =**H** R_2 = -CH_2-piperidine, -CH_2-piperidine,

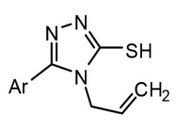




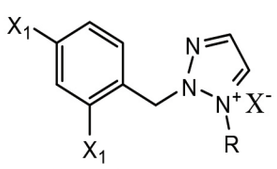
27 $\mathbf{R_1}$ =H, -CH_3



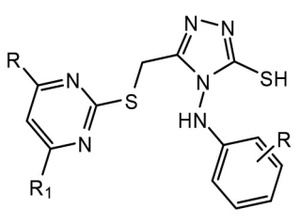
28 **Ar**= -C_6H_5-C_6H_5(p), 2-Pyridyl-1,2,4-triazole-4-yl



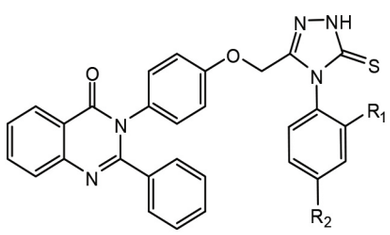
29 **Ar** = 4-OH-C_6H_4- , 2-OH-5-Cl-C_6H_4-



30 X_1- Cl, X = Br, R= $(CH_2)_{11}CH_3$, $(CH_2)_{15}CH_3$ X_1=F X= Br, R= $(CH_2)_{11}CH_3$



31 R = -CH_3, R_1= -H, R_2= p-N,N-Dimethylphenyl, 3,4-Dimethoxyphenyl, 3,4,5-Trimethoxyphenyl



32 R_1= R_2= H R_1 = H, R_2 = F R_1 = H, R_2 = NO_2 R_1 = R_2 = F

Figure 2. Structure of some triazole compounds with antimicrobial activities

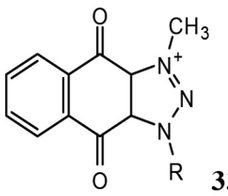
A novel class of cationic anthraquinone analogs **33a-c,** compound **33a** showed high potency (MIC<1ug/mL) and selectivity against G-positive pathogens including methicillin resistant *S. aureus* (MRSA), while modest activity against G-negative bacteria. Compound **33b** and **33c** exhibited broad antibacterial activity including MRSA and vancomycin-resistant *Enterococcus faecalis* (VRE), comparable to other available cationic antiseptics[55]. A series of coumarin based 1,2,4 triazol derivatives were exhibited antimicrobial activities in vitro against G-positive bacteria (*S. aureus*, MRSA, *B. substilis* and *M. luteus*), four G-negative bacteria (*E. coli, Proteus vulgaris, S. typhi* and *S. dysenteriae*) as well as fungi (*C. albicans, S. cerevisiae* and *A. fumigatus*). Compounds **34** and **35 were** displayed stronger antibacterial and antifungal efficacy[56].

A series of sulphanilamide derived 1,2,3 triazol compounds (**36**) were displayed *in vitro* antibacterial and antifungal activities. Compounds 4-amino-*N*-((1-dodecyl-1*H*-1,2,3-trizol-4-yl) methyl)benzenesulfonamide **36a**, 4 amino-N-((1-(2,4-dichlorobenzyl)-1*H*-1,2,3 triazol-4-yl) methyl)-4-aminobenzenesulfonamide **36b** and 4-amino-*N*-((1-(2,4-diflurobenzyl)-1*H*-1,2,3-triazol-4-yl) methyl) benzenesulfonamide **36c** were found to be most potent compounds against fungal strains[57]. A series of *N,N* bis (1,2,4 triazol-1-yl methyl) amines were exhibited antifungal activity against the budding yeast *S. cerevisiae* and antibacterial activity against *E. coli*. Compounds 2,6-bis (bis(1*H*-1,2,4-triazol-1-yl) methyl)amino)hexanoic acid **37** and *N,N* (bis ((1*H*-1,2,4-triazol-1-yl) methyl)-2 methyl propane-amine **38** were showed strong antifungal and antibacterial activity[13]. Glucosidation of some 4-amino- and 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones with 2,3,4,6-tetra-*O*-acetyl-α-d-glucopyranosyl bromide **39, 40** that gave the corresponding *N*- and *S*-β-dglucosides[58] were showed antimicrobial activity against *A. fumigatus*, *Penicillium italicum*, *Syncephalastrum racemosum*, *C. albicans*, *S. aureus*, *P. aeruginosa*, *B. subtilis*, and *E. coli*. Some 1-(5-phenylamino-[1,3,4] thiadiazol-2-yl)methyl-5-oxo-[1,2,4]triazoles **41** and 1-(4-phenyl-5-thioxo-[1,2,4]triazol-3-yl) methyl-5-oxo- [1,2,4]triazolederivatives **42** were displayed antimicrobial properties. Most compounds have antimicrobial activity against one or more microorganism, but no antifungal activity has been observed against yeast like fungi. The inhibitory effect on mycelial growth by three compounds had been observed[50].

Some 1,3,4-thiadiazol-2-ylmethyl-1,2,4-triazoles **43-45** were showed microbial activities. Some compounds of them showed good activity against a variety of microorganisms[60]. A series of 1-[1,2,4-triazol-3-yl] and 1-[1,3,4-thiadiazo l-2-yl]-3-methylthio-6,7-dihydrobenzo [*c*] thiophen-4(5*H*)ones **46** were showed *in vitro* antimicrobial activity. Some of these compounds exhibited a good activity against *S. aureus*, *S. epidermidis* and *Bacillus subtilis*[61]. A series of 4-alkyl/aryl-2,4-dihydro-5-((6-(4-bromophenyl) imidazo[2,1-b]thiazol-3-yl)methyl)-3*H*-1,2,4-triazole-3-thiones **47** were showed antibacterial and antifungal activities. These compounds were also showed antitubercular activity against *M. tuberculosis* H37Rv[63]. Formation of *N*- and *O*-propargylated quinazoline derivatives from quinazol-4-ones **48** and a series of perfluoroalkyl-1*H*, 1,2,3-triazol-4-yl substituted quinazolines were showed antimicrobial activity and identified as potential compounds[63].

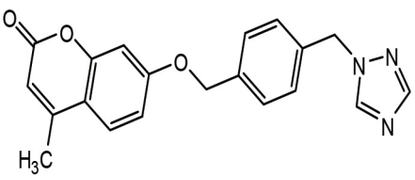
Substituted coumarin 1,2,4 triazol and sulphanilamide derived 1,2,3 triazol compounds displayed stronger antibacterial action. A series 5-(4-amino substituted-8-(trifluoromethyl) quinolin-3-yl)-4-(un)substituted phenyl-4H-1,2,4-triazole-3-thiols **(49)** from derivatives of 4-hydroxy-8-(trifluoromethyl) quinoline-3-carbohydrazide were showed antimicrobial activity against *E. coli, S. aureus, P. aeruginosa, K. pneumonia* and activity was compared with ciprofloxacin as standard drug. The compounds **49a, 49b** and **49c** showed good activity against all the bacterial strains[64]. A series of sulfanilamide-derived 1,2,3-triazole compounds (**50, 51**) were showed *in vitro* antibacterial and antifungal activities against *S. aureus, E. typhosa, P. aeruginosa, S. dysenteriae, B. subtilis, E. coli,* as well as *C. albicans* and *C. mycoderma.* The activity of the compounds was compared with the reference drug chloramphenicol. The compounds **50, 51a** and **51b** bearing dodecyl,

2,4-dichlorobenzyl and 2,4-difurobenzyl group showed the most potent antibacterial activities against all tested bacterial strains with the MIC values ranging from 32 to 128 μg/mL[65].



33a-c

a R= -$CH_2(CH_2)_6CH_3$;
b R= -$CH_2(CH_2)_{10}CH_3$;
c R= -$CH_2(CH_2)_{14}CH_3$



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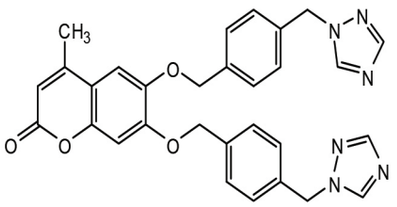

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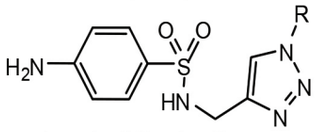
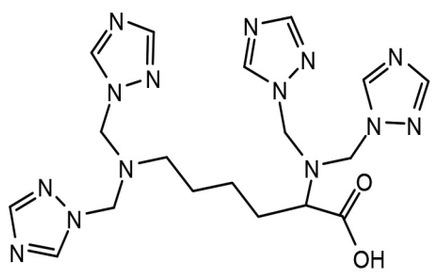


36 (**36a**) -$(CH_2)_{11}CH_3$; (**36b**);-CH_2; (**36c**); -CH_2



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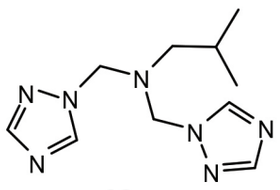

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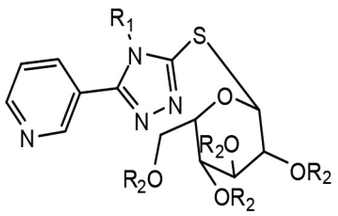

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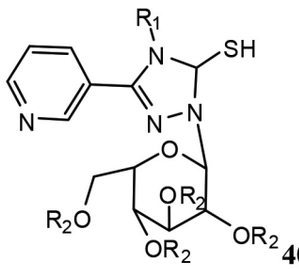
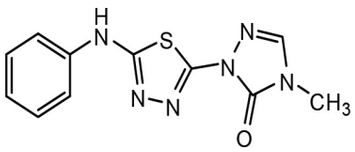


40

R_1=H,NH_2,C_6H_5CH=N,4-$CH_3C_6H_4CH$=N,4-$CH_3OC_6H_4CH$=N, 4-ClC_6H_4CH=N; R_2=$COCH_3$,H



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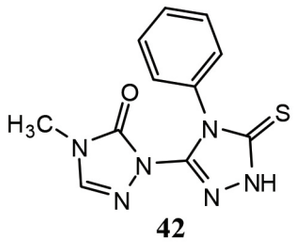

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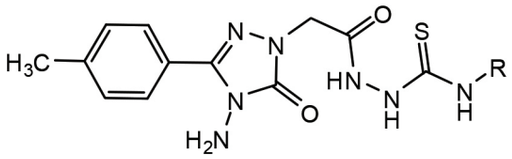

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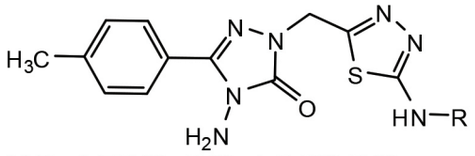
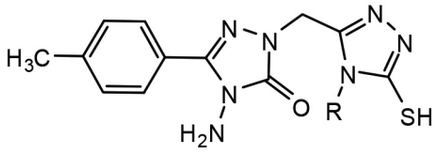


44 R=4-FC_6H_4,C_6H_5,4-$OCH_3C_6H_4$



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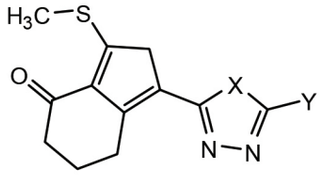
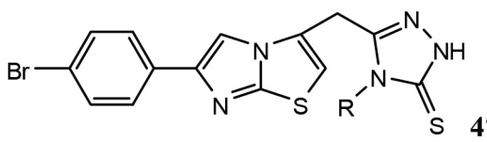


46 X = NR, S; Y = NH_2, NHR, SH, SMe



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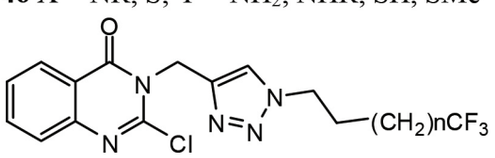
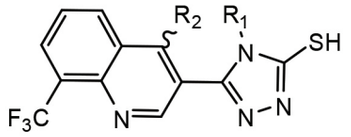
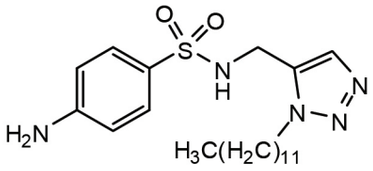


R=CH_3,C_2H_5, C_3H_7, C_4H_9, CH_2=$CHCH_2$, C_6H_5 **48**



49 $\mathbf{R_1}$= Ph, -CH_2Ph, -CH_2CH_2OMe; $\mathbf{R_2}$= substituted amines; **49a**: cyclopropyl amine, **49b**: cyclohexyl amine, **49c**: 3,3 Dimethyl butylamine. **49d**: Piperidine-4-propanol, **49e**: Morpholine, **49f**: 4-Piperidine morpholine



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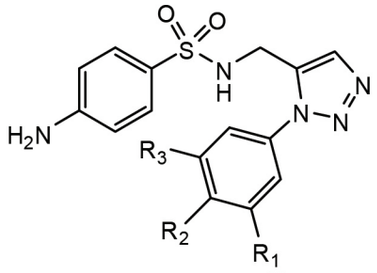


51 **51a** R_1=Cl, R_2 = H, R_3 = Cl; 5**1b** R_1 = F, R_2 = H, R_3 = F

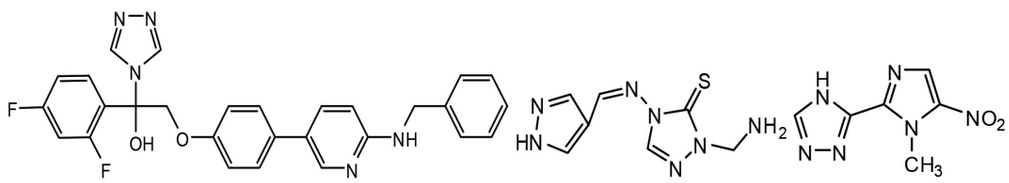
Figure 3. Structure of some triazole compounds with antimicrobial activities

A derivatives of 1-(substituted biaryloxy)-2-(2,4-difluoro phenyl)-3-(1H-1,2,4-triazol-1-yl) propan-2-ol derivatives **(52)** were showed antifungal activity against eight human pathogenic fungi in vitro. Most compounds showed activity between 4- and 64-fold higher than voriconazole against *C. albicans*. Activity suggested that introduction of a biaryloxy side chain greatly improved the antifungal activity of triazole[66]. A series of 4-[(3-substituted-1H- pyrazol- 4-yl) methylene amino]-5-substituted-2-[(4-methyl piperzine-1-yl)methyl]-2H-1,2,4-triazole-3(4H)-thiones **(53)** were showed antibacterial and antifungal activity. Some of the compounds were found to exhibit antimicrobial activity[67]. Various 5-(1-methyl-5-nitro-2-imidazolyl)-4*H*-1,2,4-triazoles **(54)** were showed *in vitro* antibacterial and antifungal activities. Two compounds exhibited significant effects against *B. subtilis* at MIC ranges of 0.5-1 µg/mL and moderate effects against *S. aureus*[68]. Various 5-(1-methyl-5-nitro-2-imidazolyl)-4H-1,2,4-triazoles **(55)** were showed in vitro antibacterial and antifungal activities. Two compounds exhibited significant effects against *B. subtilis* at MIC ranges of 0.5-1µg/mL and moderate effects against *S. aureus*[69]. A series of 3-[4-(substituted phenyl-5-thioxo-4, 5-dihydro-1*H*-1,2,4 triazole-3-ylmethoxy)-phenyl]-2-phenyl-3*H*-quinazoline-4-one **(56)** was showed antifungal activity. The compound 3-{4-[-nitrophenyl)-5-thioxo-4,5-dihydro-1*H*-[1,2,4]triazole-3-yl-methoxy]phenyl}-2-phenyl-3H-quinaolin-4-one was exhibited good activity against *A. niger*[70]. A series of compound (3) 7-(3-(1H-1,2,3-triazole-1-yl)propoxy)-4methyl-2Hchromen-2-one **(57)** was exhibited *in-vitro* antifungal activity against strain of *C. albicans*. All compounds except compound (**57a**) showed moderate antifungal activity while compound (**57c**) 7-(2-(1H-1,2,3-triazole-1-yl)-4-(4-nitrostyryl)-2H chromen-2-one showed antifungal activity as comparable to Ketoconazole[71]. Some 3-(*p*-substituted anilinoethyl)-4-(*p*-substituted phenyl)-5-thioxo-1,2,4-triazoles **(58)** were showed antifungal activity against *C. albicans* and *A. niger*[72].

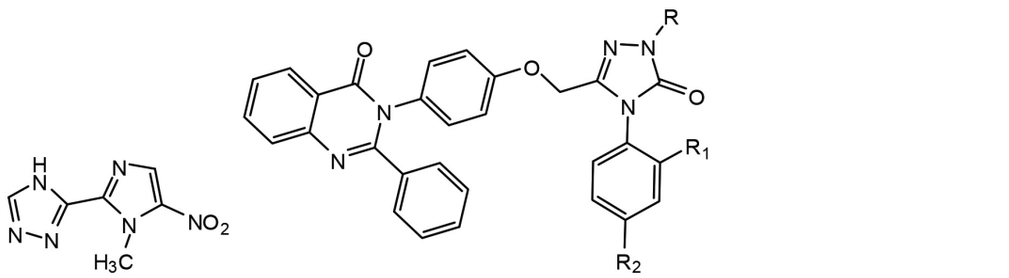
The antibacterial activity of C-5-substituted triazole-oxazolidinones **(59)** showed antibacterial activity against *Mycobacterium smegmatis*, *B. subtilis,* and *E. faecalis*. The 3-(4-acetyl-phenyl)-5-(1H-1,2,3-triazol-1-yl) methyl)-oxazolidin-2-one was showed 4-fold lower MIC value than isoniazid[73]. A series of heterocyclic systems, triazolo[4,3-a]-quinazolin-7-ones **(60)** [1,2,4,5]-tetrazino[4,3-a]-quinazolin-8-ones and indolo[2,3-c][1,2,4]-triazino[4,3-a]-quinazolin-8-ones were exhibited antibacterial activity against G-negative bacteria, *E. coli, P. aeruginosa* and G-positive bacteria e.g. *S. pneumoniae, B. subtilis*, as well as for antifungal activity against fungal stains, *C. albicans, A. fumigatus, A. flavus* and *A. niger*. Some compounds were showed potent antifungal and antibacterial activity[74]. A series of 2,4-dichloro-5-fluorophenyl

bearing thiazolotriazoles **(51)** starting from 3-(2,4-dichloro-5-fluorophenyl)-4H-1,2,4-triazole-3-thiol were exhibited potent antibacterial activity and some compounds showed significant antifungal activity[75]. The triazole substituted triazolo-pyrimidine derivatives (**62**) were showed antibacterial activity[76]. The 6,7-dihydro-1,3,4-triazolo[1,5-a]-1,3,5-triazin-2-Sulfonamides (**63**) showed herbicidal and plant growth regulating activity[77]. Some 4-allyl/amino-5-aryl-1,2,4-triazoles (**64**) were showed antibacterial and antifungal effects against *E. coli, B. subtilis, S. enteritidis, S. aureus, A. niger* and *C. albicans*[78]. The 3-[4-(4-substituted phenyl-5-thioxo-4, 5-dihydro-1H-1,2,4 triazol-3-ylmethoxy)-phenyl]-2-phenyl-3H-quinazolin-4-one (**65**) were showed *in vitro* antibacterial activity[79]. The 5-(N-substituted carboxamidomethylthio)-3-(3'-pyridyl)-1,2,4-triazole derivatives (**66**) were showed antibacterial activity[80].

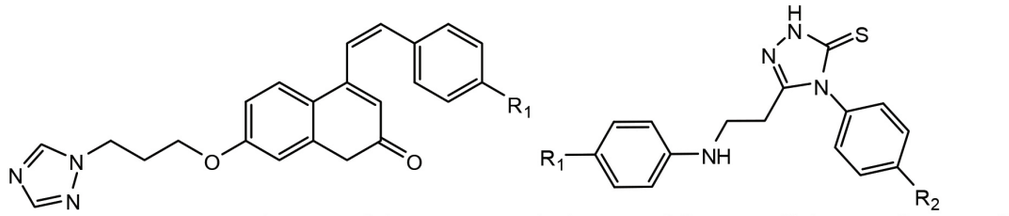
The 5-(3',4'-dihydro-2',2',8'-trimethyl-2'H-1'-benzopyran-7-yloxymethyl)-4-phenyl-1,3,4-triazole -3(4H)-thiol (**67**) was showed significant antifungal activity[81]. The 5-(N-substituted carboxamidomethylthio)–3-(3'-pyridyl)- 1,2,4-triazole derivatives (**68**) showed anti-fungal activity against *C. albicans* and *A. niger* at the concentrations of 50 and 100 µg/mL using Fluconazole as the standard[82]. A series of 3,6-disubstituted-1, 2, 4-triazolo-[3, 4-b]-1,3,4-thiadiazoles (**69**) were showed antifungal activity against *C. albicans* and *A. niger* using Ketoconazole as standard[83]. The Candida fungals were impinged by the new triazole derivatives **(70)**, showed both by *in vivo* and *in vitro* anti-fungal activity. The 1,4-di-substituted-1,2,3-triazole compounds with long alkyl chains displayed a good antifungal activity. It was more potent than the reference drugs, ketoconazole, amphoterecin B and fluconazole. The enantiomers are still under development as they are believed to have more potent activity than the racemic compounds. The compound **(71)** showed excellent activity against *C. albicans*[84,85]. A 2-substituted-5-[isopropylthiazole] clubbed 1,2,4-triazole were showed potent antifungal agent. The compound (**72),** 3-(4-Isopropyl thiazol-2-yl) -6-(4-nitrophenyl)-[1,2,4] triazolo [3,4-b][1,3, 4] thiadiazole[86] and other compounds (**73-76**) were also exhibited antifungal activity[87].



52 **53** **54**



55 **56**



57 **57a**, **57c** (R1=H,NO_2) **(58)** R_1=H, OCH_3, Br, Cl / R_2=H, CH_3, Br, Cl

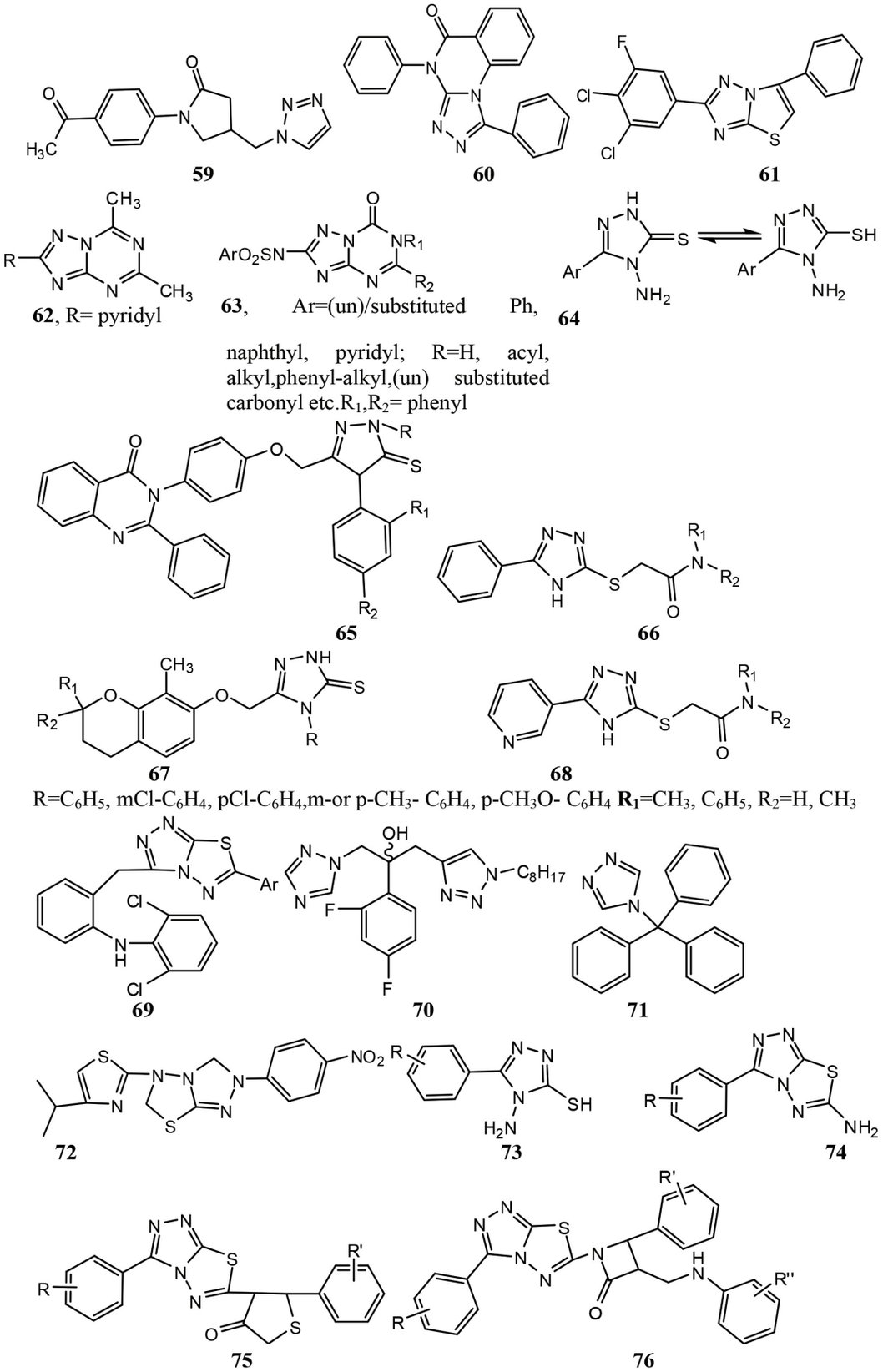


Figure 4. Structure of some triazole compounds with antimicrobial activities

3. ANTIVIRAL ACTIVITY

HIV (retrovirus) resulting in the slow depletion of immune system of the affected human beings resulting in opportunistic infections. Some compounds were evaluated for the anti-HIV activity, such as 4-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)amino]-*N*(4,6-dimethyl-2-pyrimidinyl)-benzenesulphonamide and its derivatives (**77)** were found active against replication of HIV-1 and HIV-2 in MT-4 cells[88]. Various derivatives of trisubstituted triazoles (**78)** were act as inhibitors of reverse transcriptase and the two compounds with difference in thio group position were found most active compounds[89]. The thiourea derivatives, 5-[(4-amino phenoxy) methyl]-4-alkyl/aryl-2, 4-dihydro-3H-1,2,4 triazole-3-thiones (**79**) having good activity against cox sacie virus B4, also active against the thymidine kinase positive *Varicella zoster* Virus[90]. The N-amino-1,2,3-triazole (**80**) were exhibited antiviral activity against cantalago virus. The ethyl 1-(7-phenyl-2H-3,5,6,7-tetrahydro-imidazo[2,1-c][1,2,4]triazol-3-yl) formate (**81**) was effective on human adenovirus 5 (Ad-5) and human enterovirus (Echo-9) replication and the activity against the selected DNA (Ad-5) and RNA (Echo-9) viruses and the cytotoxicity towards normal GMK (Green Monkey Kidney) cells were determined[91,92].

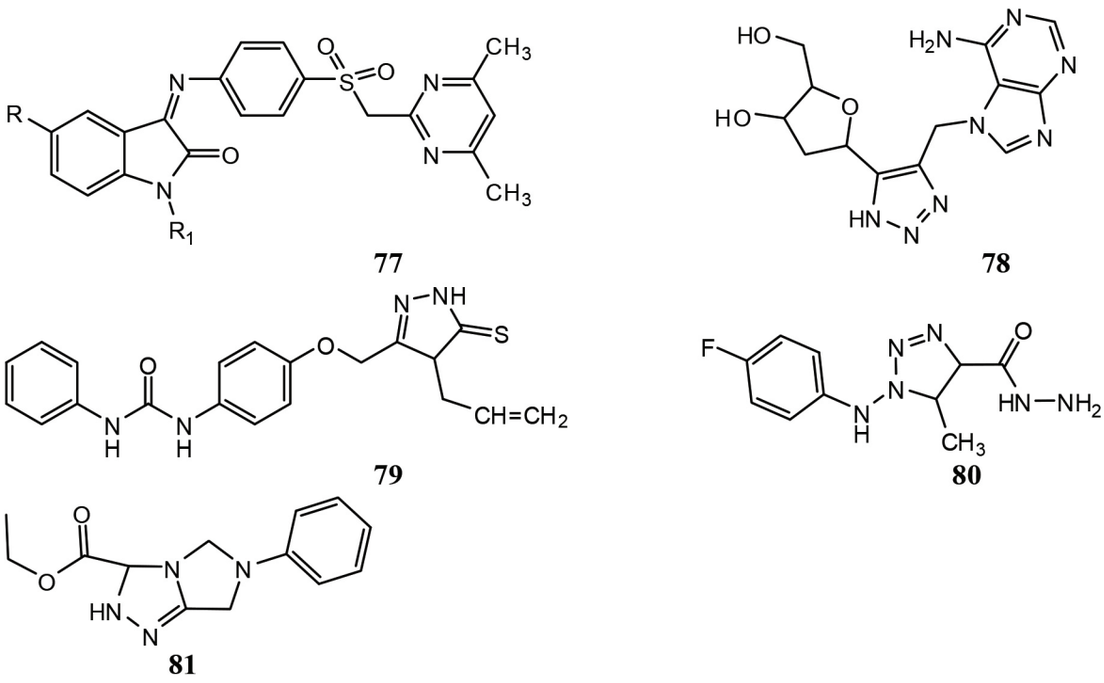


Figure 5. Structure of some triazole compounds with antiviral activities

4. CONCLUSION

Many different triazole derivatives have been prepared from its useful pharmacological activities. In the present review, reported the different pharmacological activities of triazole derivatives. Triazole derivatives possess a wide range of pharmacological activities such as anticancer, anticonvulsant, antimicrobial, antitubercular, antimalarial, anti-inflammatory, antioxidant, analgesic etc. In general triazole ring, substitution at 1,4 and 1,3 positions with electronegative group will possess more active compounds. Some triazole compounds are in therapeutic uses like, Itraconazole, Voriconazole, Fluconazole, Posaconazole (antifungal), Ribavirin (antiviral), Trapidil (antihypertensive and aasodilator), Rilmazafone (anxiolytic), Nefazodone, Trazodone (antidepressant), Estazolam (sedative-hypnotic), Rufinamide (antiepileptic), Anastrozole

(antineoplastic), Alprazolam (tranquillizer). These diverse pharmacological activities of triazole are the milestone for the new research. Modifications in triazole ring displayed valuable biological activities and these modifications can be utilized to develop more effective agents for future explorations.

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