

Triazole as Pharmaceuticals Potentials

Rakesh Kumar^{1*}, Mohd. Shahar Yar²,
Saurabh Chaturvedi³, Atul Srivastava³.

^{1,3}Pranveer Singh Institute of Technology, Kanpur, (U.P) India^{1,3}.
²Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard,
New Delhi, India.

*Corres. Author: rakeshpsit.saini@gmail.com
Mob.no. 09452075670

Abstract: In the previous years the synthesis of high nitrogen containing heterocyclic systems has been attracted to many pharmaceutical and agrochemical industries. The triazole nucleus is one of the most important heterocycles which is a feature of natural products and medicinal agents. Triazole nucleus is enjoying their importance as being the center of activity. The nitrogen containing heterocyclics are found in abundance in most of the medicinal compounds. The triazoles are said to be the isosters of imidazoles in which the carbon atom of imidazole is isosterically replaced by nitrogen. Triazole & its derivatives have a wide range of application. They are predominantly among the type of compounds used such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antihypertensive, antimalarial, antianxiety, antidepressant, and antihistaminic, antitubercular agents etc. The derivatization of Triazole ring is based on the phenomenon of bioisosterism in which replacement of oxygen of oxadiazole nucleus with nitrogen triazole analogue.

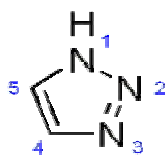
Keywords: 1,2,3-Triazole, 1,2,4-Triazole, Pharmacological Activities.

Introduction

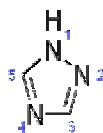
Now a day's research is concentrated towards the introduction of new and safe therapeutic agents of clinical importance. The success of imidazole as an important moiety of number of medicinal agents led to introduction of the triazoles¹. The triazoles are said to be the isosters of imidazoles in which the carbon atom of imidazole is isosterically replaced by nitrogen. Triazoles nucleus have been incorporated into a wide variety of therapeutically interesting drug candidates including anti inflammatory, CNS stimulants, sedatives, antianxiety and antimicrobial agents, Anti fungal activity. They are 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. The Triazole derivative possess a wide a range of pharmacological such as antimicrobial, analgesic, anti- Inflammatory, anti convulsant, anti neoplastic, anti malarial, anti viral, anti proliferative, and anti cancer activities. The importance of triazole derivatives lies in the field that these have good position in heterocyclic chemistry, due to its various biological activities².

Chemistry

Triazole, also known as pyrroldiazole is one of the classes of organic heterocyclic compounds containing a five-membered diunsaturated ring structure composed of three nitrogen atoms and two carbon atoms at non-adjacent positions. The simplest form of the triazole family is triazole itself. Triazole is a white to pale yellow crystalline solid with a weak, characteristic odour; it is soluble in water and alcohol, melts at 120°C and boils at 260°C. It occurs as a pair of isomeric chemical compounds 1,2,3- triazole, 1, and 1,2,4-triazole (Fig.1), 2 with molecular formula $C_2H_3N_3$, and a molecular weight of 69.06 . The two isomers are:



1,2,3- triazole



1,2,4- triazole

Chemical structures of 1,2,3 and 1,2,4-triazole.

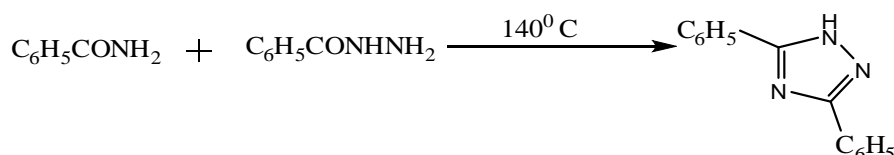
Table-1

Properties of 1, 2, 3-triazole		Properties of 1, 2, 4-triazole	
Molecular formula	$C_2H_3N_3$	Molecular formula-	$C_2H_3N_3$
Molar mass	69.0654	Molar mass -	69.0654
Boiling point	203 °C	Boiling point-	260
Melting point	23-25 °C	Melting point -	120-121°C
Density	1.192 g/cm ⁻³	Density -	1.394 g/cm ⁻³
Appearance	colourless liquid	Appearance	white solid
Solubility in water	very soluble	Solubility in water	very soluble
Basicity (pK_b)	9.4	Basicity -(pK_b)	10.3
Acidity (pK_a)	1.2	Acidity -(pK_a)	2.2
Vapour Pressure	0.4 mmhg (25°c)	Vapour Pressure	0.02 mmhg (25°c)

Method of synthesis:

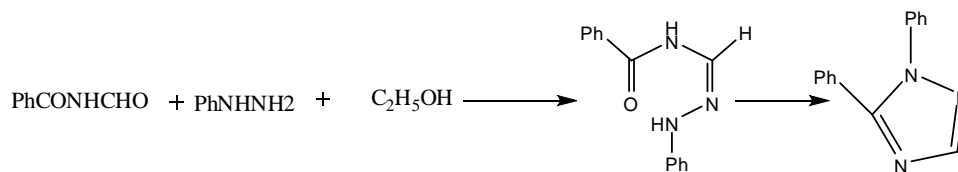
❖ Pellizari Reaction

The synthesis of 1,2,4-triazole derivatives by the mixture of amide and acyl hydrazide is generally referred to as the Pellizzari reaction. It has been reported that heating the mixture of formamide and hydrazine hydrochloride with KOH yield of 1,2,4-triazole. For example benzamide and benzoyl hydrazide gave 3,5-diphenyl-1,2,4-triazole⁴.

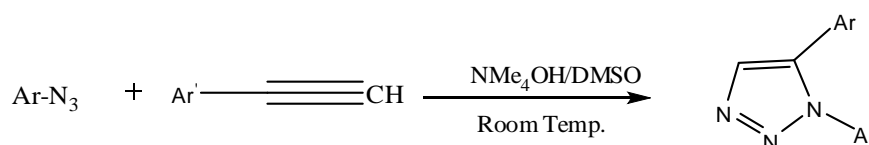


❖ Einhorn- Brunner Reaction

The synthesis of 1,2,4-triazoles by condensation between hydrazines or mono substituted hydrazine and diacylamines in the presence of weak acid is known as the Einhorn–Brunner reaction. For example N formyl benzamide and phenyl hydrazine gave 1,5-diphenyl-1,2,4-triazole⁵.



- ❖ 1,5-Diarylsubstituted 1,2,3-triazoles are formed by aryl azides and alkynes in DMSO in the presence of a catalytic amount of tetra alkyl ammonium hydroxide. The reaction is simple, does not require a metal catalyst⁶.

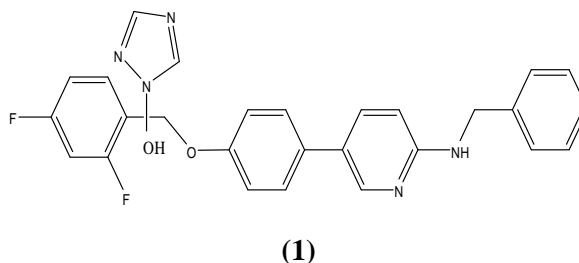


Pharmacological activities ;

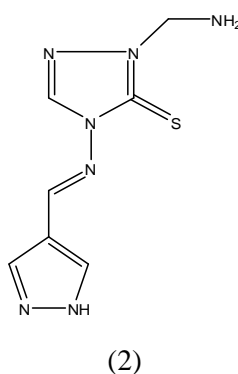
The triazole are versatile and has been featured in a number of clinically used drugs. The most relevant and recent studies have revealed that triazole derivatives have a broad spectrum pharmacological activity which can be classified into the following categories:

Antimicrobial activities

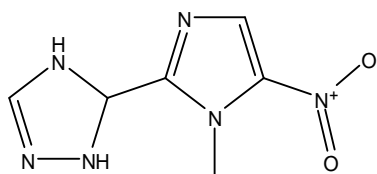
Liu et al. synthesized a derivatives of 1-(substituted biaryloxy)-2-(2,4-difluoro phenyl) -3-(1H-1,2,4-triazol-1-yl) propan-2-ol derivatives, **(1)** and their antifungal activity was evaluated against eight human pathogenic fungi in vitro. Seventeen compounds showed activity between 4- and 64-fold higher than voriconazole against *Candida albicans*. Structure-activity relationship clearly suggested that introduction of a biaryloxy side chain greatly enhanced the antifungal activity of triazole⁷.



Isloor AM et al. screened a series of new 4-[(3-substituted-1H- pyrazol- 4-yl) methylene amino]-5-substituted-2-[(4-methylpiperzine-1-yl) methyl]-2H-1,2,4-triazole-3(4H)-thiones **(2)** for their antibacterial and antifungal activity. Some of the compounds were found to exhibit antimicrobial activity⁸.



Shafiee et al. synthesized Various 5-(1-methyl-5-nitro-2-imidazolyl)-4H-1,2,4-triazoles (**3**) were evaluated *in vitro* antibacterial and antifungal activities. Two compounds exhibited significant effects against *Bacillus subtilis* at MIC ranges of 0.5-1 µg/mL and moderate effects against *Staphylococcus aureus*⁹.

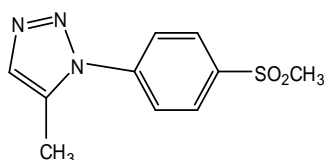


5-(1-methyl-5-nitro-2-imidazolyl)-4H-1,2,4-triazolen

(3)

Anti-inflammatory Activity-

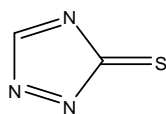
Wuest et al. synthesised a series of 1,4- and 1,5-diaryl substituted 1,2,3-triazoles (**4**). All compounds were tested for *in vitro* cyclooxygenase (COX) assays to determine the combined electronic and steric effects on COX-1 and COX-2 inhibitory potency and selectivity. The high COX-2 inhibition potency of some 1,2,3-triazoles having a vicinal diaryl substitution pattern along with their ease in synthesis through versatile Ru(II)-catalysed click chemistry make this class of compounds interesting candidates for further design and synthesis of highly selective and potent COX-2 inhibitors¹⁰.



(4)

5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-1,2,3-triazole

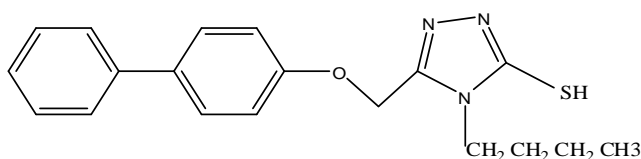
Abdel-Rahman et al. synthesised a series of new 1,2,4-triazole-5-thione derivatives (**5**). The newly synthesised compounds were evaluated for their anti-inflammatory and analgesic activities. Some compounds exhibited comparable anti-inflammatory activity to that of Indomethacin where as other compounds were more potent analgesics than acetyl salicylic acid¹¹.



1,2,4-triazole-5-thione

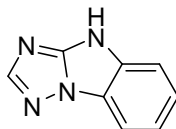
(5)

Amir M et al. synthesized a series of compound 5-[(Biphenyl-4-yloxy) -methyl]-4-nsubstituents-3-marcpto-(4H)-1,2,4-triazole. Synthesized compounds were screened for anti-inflammatory activity out of the synthesized compounds 5-[(Biphenyl-4-yloxy) methyl]-4-n-butyl-3-marcpto-(4H)-1,2,4-triazole (**6**) showed potent anti-inflammatory activity¹².



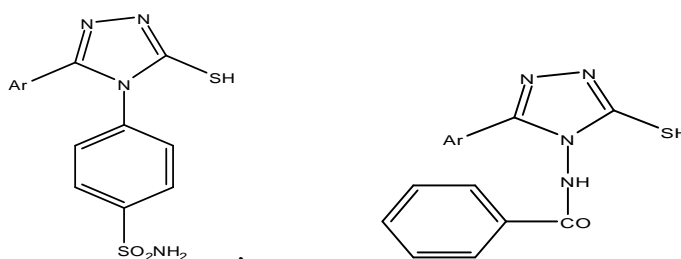
(6)

Mohamed et al. screened some new derivatives of 1,2,4-triazolo[2,3-a]benzimidazoles (**7**) for their possible anti-inflammatory and analgesic effect and most of these compounds showed potent and significant results compared to Indomethacin. Moreover, ulcerogenicity and the median lethal dose of the most active compound were determined in mice¹³.



(7)

Pattan Shasikant a new series of 1,2,4-triazole derivatives of 5-Mercepto- 1,2,4-triazole derivatives(**8**) have been synthesized & evaluated anti-inflammatory activity of when compared with standard drug¹⁴.

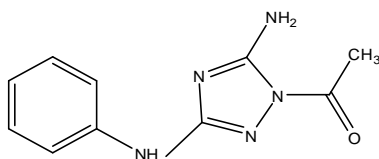


5-Mercepto- 1,2,4-triazole derivatives

(8)

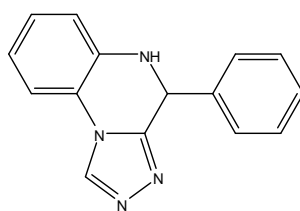
Anti Cancer activity

Lin et al. reported a series of 1-acyl-1H-[1,2,4]triazole-3-5-diamine analogues (**9**) and found them to be cyclindependent kinase (CDK) inhibitors. These compounds demonstrated potent and selective CDK1 and CDK2 inhibitory activities and inhibited in vitro cellular proliferation in various tumor cells and also demonstrated in vivo efficacy in human melanoma A375 xenograft model in nude mice¹⁵.



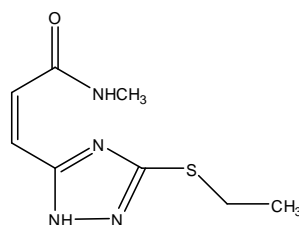
(9)

El-Hawash et al. synthesized a novel series of quinoxalines derived 1-substituted-4-phenyl-1,2,4-triazolo[4,3-a]quinoxalines (**10**) in order to evaluate their antitumor activity. Preliminary screening revealed that some compounds exhibited moderate to strong growth inhibition activity on various tumor panel cell lines between 10⁻⁶ to 10⁻⁵ molar concentrations. One compound showed selectivity towards CNS-cancer SF-639, leukemia CCRFCEM, and melanoma SK-MEL-5¹⁶.



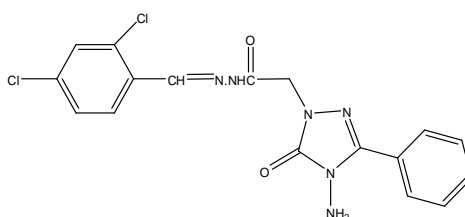
(10)

Pachuta-Stec et al. synthesised some new N-substituted amides of 3-(3-ethylthio-1,2,4-triazol-5-yl)propenoic acid (**11**) and screened them for their anticancer activity. Three compounds of this series were found to be evidently effective against lung cell line *in vitro*. The distinctly marked antiproliferative effect of two compounds in breast carcinoma cells *in vitro* was ascertained. Moreover, the lowest cytotoxicity of one compound against the normal skin fibroblast cell line and breast carcinoma cell *in vitro* after 24- and 48-hours of incubation period was noticed in this study¹⁷.



(11)

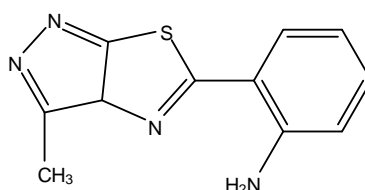
Demirbas et al. synthesized a series of compounds 4-amino-3-substituted-5-oxo-4,5-dihydro-[1,2,4] tri-azole-1-yl acetic acid 2 ,4-dichloro-benzylidene-hydrazide derivative (**12**) and screened for their anti-cancer activity. The compound 4-amino-3-phenyl-5-oxo-4,5-dihydro-[1,2,4] tri-azole-1-yl acetic acid 2 ,4-dichloro-benzylidene-hydrazide showed a potent therapeutic activity for the treatment of breast cancer¹⁸.



(12)

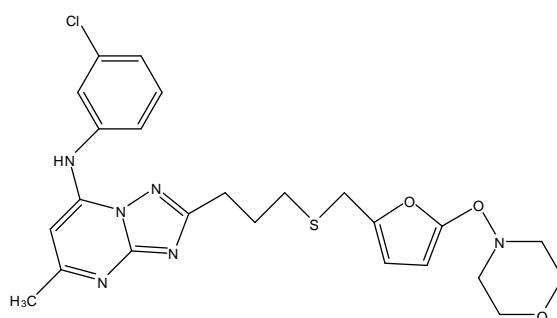
2-(4-amino-5-oxo-3-phenyl-4,5-dihydro-1H-1,2,4-triazol-1-yl)-N'-(2,4-dichlorobenzylidene)acetohydrazide

Zhai et al. synthesized a series of novel N-anilino-5-methyl-2-(3-(5 (alkyl amino methyl)furan-2-yl-methylthio) propyl)-[1,2,4]triazolo-[1,5-a]pyrimidine-7-amine derivatives (**13**) and evaluated *in vitro* cytotoxicity against two cancer cell lines, Bel-7402 and HT-1080. One compound possessed marked cytotoxicity and emerged as a lead compound. The activity was found to depend strongly on the substitution pattern of the side chains at C-2 position, and 4-trifluoromethylanilino substituent at C-7 position was an option for anticancer potency¹⁹.

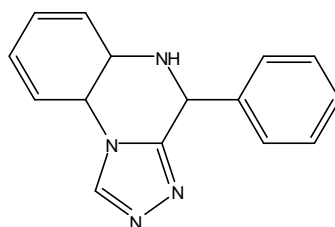


(13)

Ibrahim et al. synthesized a new series of 3,6- disubstituted [1,2,4]triazolo[3,4-b]thiadiazole derivatives (**14**). The newly synthesised compounds were evaluated for their cytotoxic activity against a panel of 60 human cancer cell lines. Some of the derivatives showed inhibitory effects on the growth of a wide range of cancer cell lines generally at the 10^{-5} M level and in some cases at concentrations of 10^{-7} M. In this assay, the antitumour activity of the newly synthesised compounds could not be interpreted in terms of tyrosine kinase inactivation but more likely as a relatively broad specificity for the ATP-binding domain of other kinases²⁰.

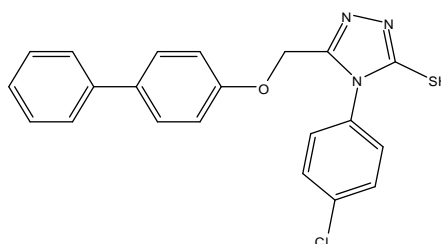
**(14)**

El-Hawash et al. synthesized a novel series of quinoxalines derived 1-substituted-4-phenyl-1,2,4-triazolo[4,3-a] quinoxalines (**15**) and evaluate their antitumour activity. Preliminary screening revealed that some compounds exhibited moderate to strong growth inhibition activity on various tumour panel cell lines between 10^{-6} to 10^{-5} molar concentrations. One compound showed selectivity towards CNS-cancer SF-639, leukemia CCRFCM, and melanoma SK-MEL-5²¹.

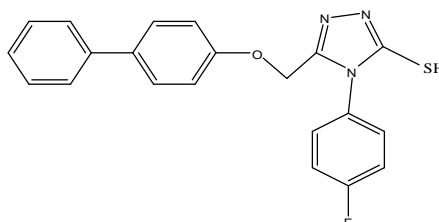
**(15)**

Analgesic Activity

Mohamed et al. screened some new derivatives of 1,2,4- triazolo[2,3-a]benzimidazoles (**16**), for their possible anti-inflammatory and analgesic effect and most of these compounds showed potent and significant results compared to indomethacin. Moreover, ulcerogenicity and the median lethal dose of the most active compound were determined in mice; and found to be 275 mg kg^{-1} ²².

**(16)**

Amir M et al. synthesized a series of 5-[(Biphenyl-4-yloxy) methyl]-4-n-substituents-3-mercapto-(4H)-1,2,4-triazole. Its derivatives such as 5-[(Biphenyl-4-yloxy) methyl]-4- fluorophenyl-3-mercapto-(4H)-1,2,4-triazole (**17**) screened for the analgesic activity. And that compound showed analgesic activity ranging from 16.9% to 72.8%, whereas the standard drug flurbiprofen showed 69.5% inhibition²³.

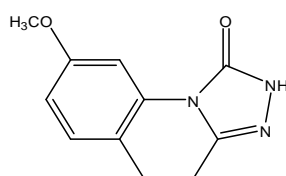


(17)

Anti convulsant Activity

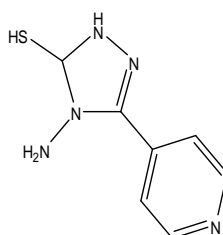
Epilepsy is a common neurological disorder and a collective term given to a group of syndromes that involve spontaneous, intermittent, abnormal electrical activity in the brain. The pharmacotherapy of epilepsy has been archived during the last decade. Furthermore, although for the last twenty years new antiepileptic drugs have been introduced into clinical practice, the maximal electroshock (MES) test and the subcutaneous pentylene tetrazole (scPTZ) test are the most widely used animal models of epilepsy to characterize the anticonvulsant activity.

Sun et al. screened a series of 8-alkoxy-4,5-dihydro-[1,2,4] triazole[4,3-a]quinoline-1-one derivatives (**18**) for their anticonvulsant activities. The tests demonstrated that 8-hexyloxy-4,5-dihydro-[1,2,4]triazole[4,3-a]quinoline-1-one and 8-heptyloxy-4,5-dihydro-[1,2,4] triazole[4,3-a] quinoline-1-one were the most potent anticonvulsants, having many fold better activity than that of drugs such as phenytoin, carbamazepine, phenobarbital and valproate²⁴.



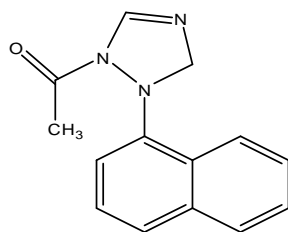
(18)

Pandeya et al. synthesised various Schiff bases such as N-[4-(4-chlorophenyl-thiazol-2-yl)] semicarbazides and 3-(4-pyridyl)-4-amino-5-mercapto-4(H)-1,2,4-triazoles (**19**).The compounds were evaluated for anticonvulsant and neurotoxic properties. These compounds emerged as the most active analogues showing anti-MES and anti-PTZ activities and better than valproic acid. All the compounds showed lower neurotoxicity than phenytoin and carbamazepine²⁵.

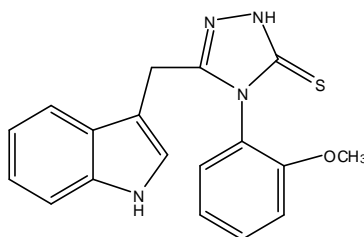


(19)

Karakurt et al. evaluated oxime and oxime ether derivatives of [1-(2-naphthyl)-2-(1,2,4-triazol-1-yl)ethanone] (**20**) as potential anticonvulsant compounds. The anticonvulsant activity of the compounds was determined by maximal electroshock and subcutaneous metrazole tests in mice and rats. Neurotoxicity was determined by the rotarod test in mice and the positional sense test, gait and stance test in rats. Although most of the O-alkyl substituted oxime ethers exhibited anticonvulsant activity, the O-arylalkyl substituted compounds were found to be inactive in the screening paradigms²⁶.

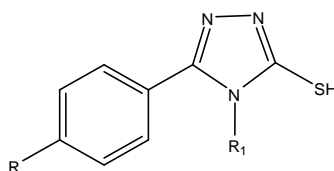
**(20)**

Siddiqui et al. synthesized a series of new 5-(1*H*-indol-3-yl)methyl-4-(substituted aryl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thiones (**21**) for their anticonvulsant activities in the MES model and compared them with the standard drugs such as phenytoin sodium and carbamazepine. Some compounds showed comparable MES activity to phenytoin and carbamazepine. One compound was found to be more potent than carbamazepine and also showed lower neurotoxicity than phenytoin²⁷.

**(21)**

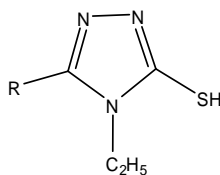
Hypoglycemic Activity

Pandeya et al. Synthesized various Substituted-1, 2, 4-Triazoles (**22**) also show hypoglycemic activity like 5-(substituted aryl), 4-(alkyl, 3-mercapto, 1,2,4-Triazole show hypoglycemic agents²⁸.

**(22)**

R = CH₃, C₂H₅, Cl, F, NO₂, NH₂ (Hypoglycemic agents)
R₁ = CH₃, C₂H₅, C₃H₇, C₄H₉

Husain et al. Synthesized 5-(substituted aryl), 4-ethyl, 3-Mercapto-1, 2, 4-triazole derivatives (**23**) show hypoglycemic activity²⁹.

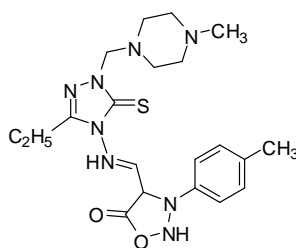


(23)

(Substituted hypoglycemic activity)

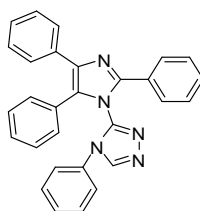
Anthelmintic Activity

Rahimani et al. synthesized some new mannich derivatives of 1-aminomethyl-3-(substituted)-4-(3-aryl-4-sydnonlydiene)-amino-1,2,4-triazol-5-thiones (**24**). Few compounds from this series were screened for their anthelmintic activity. Most of the compounds tested showed promising activity comparable with that of the standard Piperazine citrate³⁰.



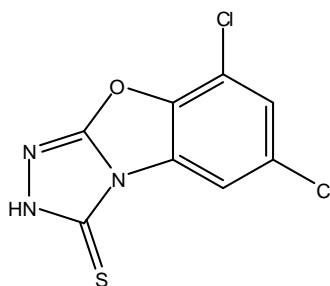
(24)

Kharb et al. synthesized a novel series of imidazole containing triazole (**25**) derivatives. All the synthesized compounds were evaluated for their anthelmintic activity against Indian earthworms (*pheretima posthuma*) at different concentrations of 0.150% and 0.300% w/v by using Albendazole as standard drug. Most of the compounds of this series have shown anthelmintic potential when compared with standard drug³¹.



(25)

Vishnumurthy KA et al. Synthesized a novel series of 6,8-dichloro [1,2,4] triazolo [3,4-*b*] [1,3] benzoxazole-3(2*H*)-thione (**26**). All synthesized compounds are screened for *in vitro* anthelmintic activities; compounds are subjected to molecular docking studies for the binding to α -Tubulin, target protein elite to the parasites. Some Compounds exhibited potential radical scavenging capacity with good anthelmintic activity. In molecular docking study also, compounds showed minimum binding energy and have good affinity toward the active pocket thus, they may be considered as good inhibitor of α -Tubulin. Some Compounds exhibited potential anthelmintic activities³².

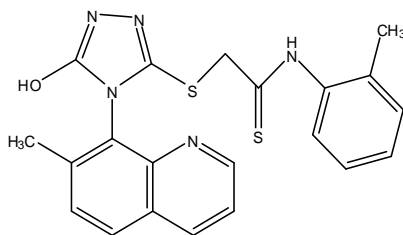


(26)

6,8-dichloro [1,2,4]triazolo [3,4-b] [1,3]benzoxazole-3(2H)-thione

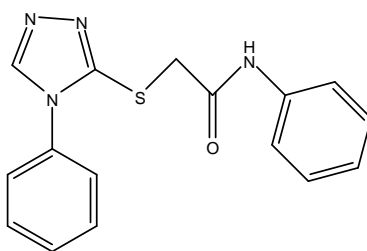
Antiviral Activity

Wang et al. reported a novel sulphanyltriazole (**27**) as an HIV-1 non-nucleoside reverse transcriptase inhibitor via high through put screening (HTS) cell-based assay. Chemical modifications and molecular modelling studies were carried out to establish its SAR and to understand its interactions with the enzyme. These modifications led to the identification of sulphanyl triazoles with low nanomolar potency for inhibiting HIV-1 replication and promising activities against selected NNRTI resistant mutants. These novel and potent sulphanyl triazoles could serve as advanced leads for further optimization³³.



(27)

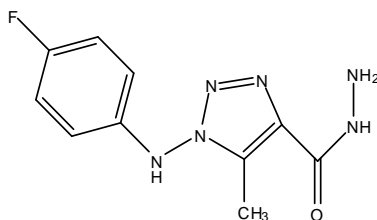
De La Rosa et al. synthesised a new series of 1,2,4-triazoles (**28**) tested against several NNRTI-resistant HIV-1 isolates. Several of these compounds exhibited potent antiviral activities against efavirenz- and nevirapine-resistant viruses, containing K103N and/or Y181C mutations or Y188L mutation³⁴.



(28)

Jordao et al. described the antiviral evaluation of new N-amino-1,2,3-triazole derivatives, 1-(substituted phenylamino)- 5-methyl-1*H*-[1,2,3]-triazole-4-carboxylic acid ethyl esters, and 1-(4-substituted-phenylamino)-

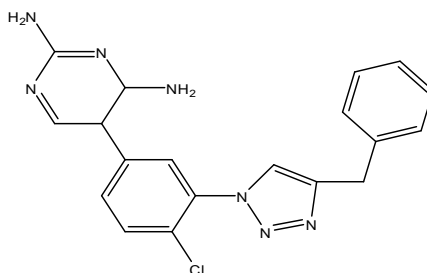
5- methyl-1*H*-[1,2,3]-triazole-4-carboxylic acid hydrazides on Cantagalo virus replication. 1-(4-Fluoro-phenyl amino)- 5-methyl-1*H*-[1,2,3]-triazole-4-carboxylic acid hydrazide (**29**) exhibited significant antiviral effect³⁵.



(29)

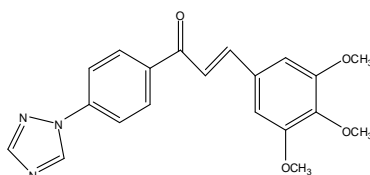
Antimalarial Activity

Chan et al. reported a structure-based design project to optimise activity, species selectivity and pharmaceutical properties of triazenylpyrimethamine TAB (IC₅₀= 0.17 M; rat liver DHFR IC₅₀/*P. carinii* DHFR IC₅₀=114). This concern led them to design, synthesise and evaluate four new series of pyrimethamine derivatives bearing triazole (**30**) triazolium, triazinium and amino moieties at the 3'-position of para-chlorophenyl ring. Such stabilised 'triazene' derivatives address potentially compromised pharmaceutical profile of TAB and the 3'-amino substituted agents afford conformationally flexible substitutes³⁶.



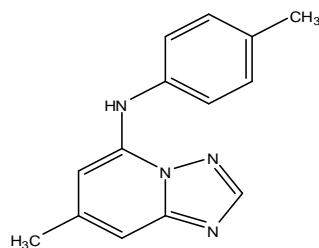
(30)

Mishra et al. Synthesized a series of novel 1,3-diaryl propenone derivatives (**31**) and their antimalarial activity *in vitro* against asexual blood stages of human malaria parasite, *Plasmodium falciparum*. Chalcone derivatives were prepared *via* Claisen- Schmidt condensation of substituted aldehydes with substituted methyl ketones. The chloro-series, 1,2,4-triazole substituted chalcone was found to be the most effective in inhibiting the *in vitro* growth of *P. falciparum* *in vitro* while pyrrole and benzotriazole substituted chalcones showed relatively less inhibitory activity. This is probably the first report on antiplasmodial activity of chalcones with azoles on acetophenone ring³⁷.



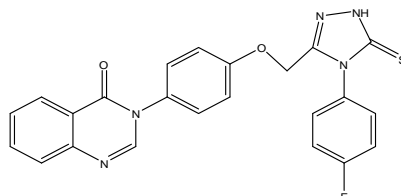
(31)

Gujjar et al. recently synthesized phenyl-substituted triazolopyrimidines (**32**) leading to identification of analogs with low predicted metabolism in human liver microsomes and which showed prolonged exposure in mice. The most active single substituted compounds in the series contained para substituents, combinations of para and meta substitutions on phenyl ring attached to triazole nucleus yielded compounds with the best antimalarial activity. One compound containing para-trifluoro methyl phenyl group suppressed growth of *P. berghei* in mice after oral administration³⁸.



(32)

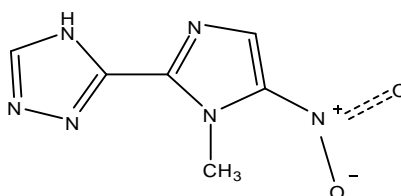
Havaladar et al. newly synthesized compounds was evaluated and sensitivity of chloroquine-resistant *Plasmodium falciparum* malarial parasite to *in vitro* by using triturated Hypoxanthine incorporation assay. The compounds were tested for antimalarial activity and only one compound that is 3-{4-[4-(4-fluoro-phenyl)-4*H*-[1,2,4]triazol-3-yl-methoxy]-phenyl}-2-phenyl-3*H*-quinazolin-4-one (33) was found to be most active against *Plasmodium falciparum* strains and its 50% inhibitory concentration IC₅₀ value was 1.2M³⁹.



(33)

Anti fungal activity

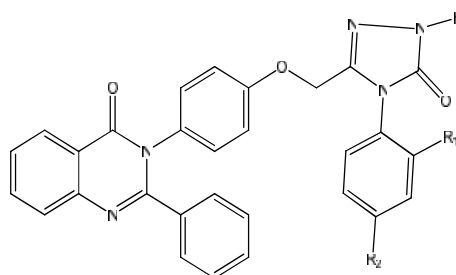
Shafiee et al. synthesized Various 5-(1-methyl-5-nitro-2-imidazolyl)-4*H*-1,2,4-triazoles (34) were evaluated *in vitro* by Shafiee et al for their antibacterial and antifungal activities. Two compounds exhibited significant effects against *Bacillus subtilis* at MIC ranges of 0.5-1μg/mL and moderate effects against *Staphylococcus aureus*⁴⁰.



(34)

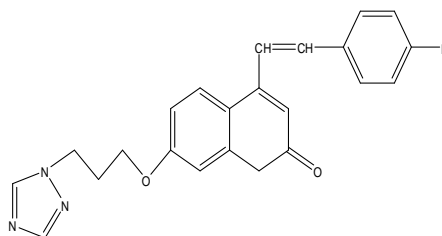
Chemical structure of 5-(1-methyl-5-nitro-2-imidazolyl)-4*H*-1,2,4-triazole.

Freddy et al. synthesized a series of 3-[4-(substituted phenyl)-5-thio-4,5-dihydro-1*H*-1,2,4 triazole-3-yl-methoxy]-phenyl]-2-phenyl-3*H*-quinazolin-4-one (35) screened for antifungal activity. The compound (2c) 3-{4-[-nitrophenyl]-5-thio-4,5-dihydro-1*H*-[1,2,4]triazole-3-yl-methoxy]phenyl}-2-phenyl-3*H*-quinaolin-4-one exhibit good activity against *Aspergillus niger*⁴¹.



(35)

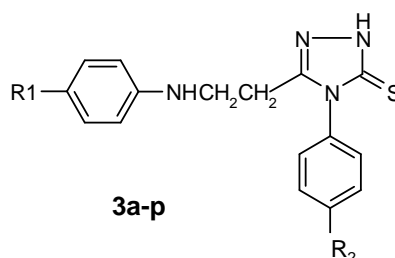
Kokil et al. have synthesized a series of compound (3) 7-(3-(1H-1,2,3-triazole-1-yl)propoxy)-4-methyl-2H-chromen-2-one (**36**) and screened for *in-vitro* antifungal activity against strain of *Candida albicans*. All compounds except compound (3a) showed moderate antifungal activity while compound (3c) 7-(2-(1H-1,2,3-triazole-1-yl)-4-(4-nitrostyryl)-2H-chromen-2-one which is nitro substituted at Para-position showed antifungal activity as comparable to Ketoconazole⁴².



Compd. 3a,3c (R₁=H,NO₂)

(36)

Siddiqui A A et al. Some new 3-(*p*-substituted anilinoethyl)-4-(*p*-substituted phenyl)-5-thioxo-1, 2, 4-triazoles (**37**) 3a-p are synthesized and evaluated for antifungal activity against *Candida albicans* and *Aspergillus niger*⁴³.

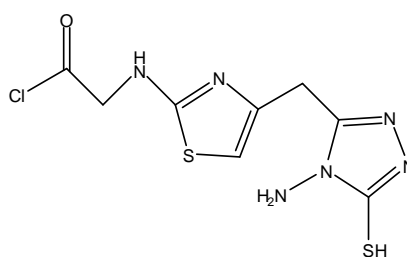


(37) R₁=H, OCH₃, Br, Cl / R₂=H, CH₃, Br, Cl

Anti Tubercular agents

Tuberculosis (TB) is a bacterial infection caused by a germ called *Mycobacterium tuberculosis*. The bacterium usually attacks the lungs, but they can also damage other parts of the body.

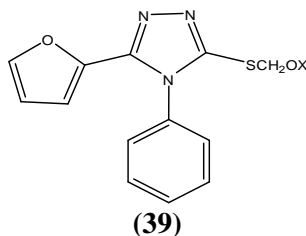
Shiradkar et al. synthesised a novel thiazolyl triazole derivatives (**38**) with the developing novel molecules with improved potency for treating *Mycobacterium tuberculosis* H37Rv strain infections and with decreased drug resistance. They also investigated them for their antimycobacterial activities. Many compounds have shown promising activity against tuberculosis⁴⁴.



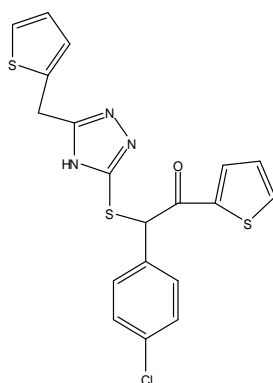
(38)

2-(4-((4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)methyl)thiazol-2-ylamino)acetyl chloride

Polya JB Substituted 1, 2, 4-triazoles also show anti tubercular activities like- [5-(2-furyl)-1, 2, 4-triazoles-3yl thio] acehydrazide (**39**) and related compounds show anti-tubercular activities. Mannich-bases of substituted triazoles are also formed which are good antibacterial agents. Some Schiff's bases of triazoles with isotin are also found⁴⁵.

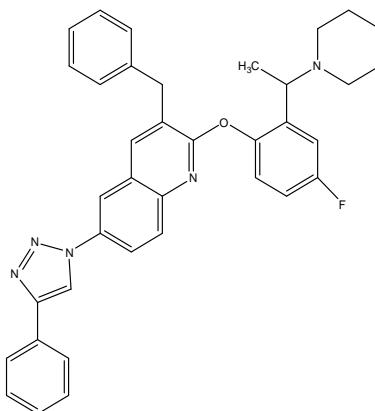


Kaplansikli et al. synthesised some novel 3-alkylsulphanyl-1, 2,4- triazole derivatives (**40**) and evaluated them for antituberculosis activity. Activity of the compounds was determined by broth micro dilution method. The micro plate Alamar blue assay, in BACTEC 12B medium and results were screened *in vitro* using the BACTEC 460 radiometric system against *Mycobacterium tuberculosis* H27Rv (ATCC 27294) at 6.25 µg/mL and the tested compounds showed considerable inhibition ranging from 58-84⁴⁶.



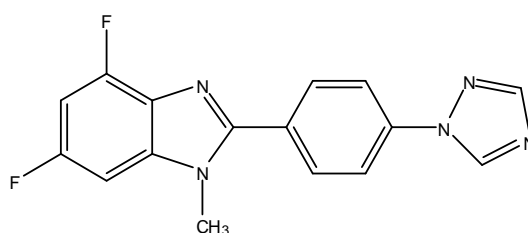
2-(4-chlorophenyl)-1-(thiophen-2-yl)-2-(5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-ylthio)ethanone
(40)

Upadhyaya et al. designed a new series of 20 quinoline derivatives possessing triazolo (**41**) ureido and thioureido substituents and evaluated their antimycobacterial properties. Three compounds inhibited *Mycobacterium tuberculosis* H37Rv up to 96%, 98% and 94% respectively, at a fixed concentration of 6.25 µg/mL. Minimum inhibitory concentration of 3.125 µg/mL was observed for two compounds while for one compound it was found to be 6.25 µg /mL. Molecular docking calculations suggest critical hydrogen bonding and electrostatic interactions between polar functional groups (such as quinoline-nitrogen, ureacarbonyl and hydroxyl) of anti-mycobacterial (anti-TB) compounds and amino acids (Arg186 and Glu 61) of ATP synthase of *M. tuberculosis* could be the probable reason for observed anti-mycobacterial action⁴⁷.



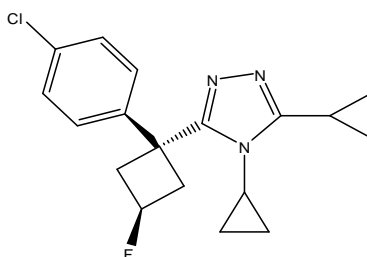
(41)

Jadhav et al. studied a series of novel 2-[4-(1*H*-[1,2,4]-triazol-1-yl)phenyl]-1-substituted-4,6-difluoro-1*H*-benzo[d]imidazole derivatives (**42**) for their preliminary *in-vitro* antibacterial activity against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella typhus* and then these compounds were screened for their antitubercular activity against *Mycobacterium tuberculosis* H37Rv strain by broth microdilution assay method. The antibacterial data suggested that the analogues with electronegative substituents emerged as the most promising antimicrobials. A few of the selected analogues are under further evaluation for secondary antitubercular screening, as they have shown better activity when compared to rifampin⁴⁸.

**(42)**

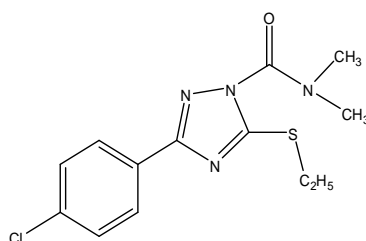
Antidiabetic activity

Zhu et al. demonstrated that 3-(phenylcyclobutyl)-1,2,4-triazole derivatives (**43**) show reduction in the blood glucose and lipid levels by the inhibition of 11 β -hydroxysteroid dehydrogenase type I (11 β -HSDI)⁴⁹.

**(43)**

3-(1-(4-chlorophenyl)-3-fluorocyclobutyl)-4,5-dicyclopropyl-4*H*-1,2,4-triazole

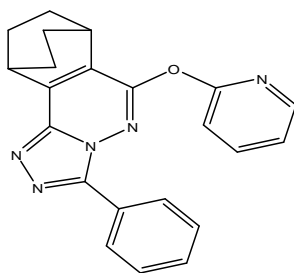
Ebdrup et al. studied four new classes of carbamoyltriazoles (**44**) to demonstrate the central role of the intracellular enzyme hormone-sensitive lipase (HSL) in regulating fatty acid metabolism for the treatment of insulin resistant and dyslipidemic disorders. On the basis of a lead structure from high throughput screening, they identified methyl-phenyl-carbamoyl-triazoles as potent and efficacious HSL inhibitors to show their antidiabetic activity⁵⁰.

**(44)**

3-(4-chlorophenyl)-5-(ethylthio)-*N,N*-dimethyl-1*H*-1,2,4-triazole-1-carboxamide

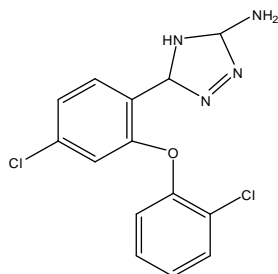
Anti anxiety activity

Carling et al. synthesized and evaluated 6-benzyloxy-3-(4-methoxy) phenyl-1,2,4-triazolo [3,4-a]phthalazine (**45**) as a ligand with binding selectivity for the gamma-aminobutyric acid-A (GABA-A) alpha 3- and alpha 5-containing receptor subtypes over the GABA-A alpha 1 subtype. Methyl substitution of the benzo-fused ring at the 7-, 8- and 10-positions resulted in increased efficacy, although selectivity was abolished. its selectivity is limited, its good pharmacokinetic profile in the rat made it a useful pharmacological tool to explore the effect of a gamma-amino butyric acid-A alpha 2/alpha 3 agonist *in vivo*⁵¹.



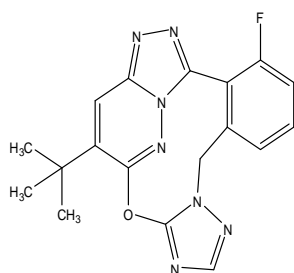
(45)

Akbarzadeh et al. synthesised a series of new 5-substituted analogues of 4*H*-3-(2-phenoxy) phenyl-1,2,4-triazole and its chlorinated derivatives (**46**). Conformational analysis and superimposition of energy minima conformers of the compounds on estazolam, a known benzodiazepine receptor agonist, revealed that the main proposed benzodiazepine pharmacophores were well matched. Rotarod and pentylenetetrazole-induced lethal convulsion tests showed that the introduction of an amino group in position 5 of 1,2,4-triazole ring especially in chlorinated derivatives had the best effect which was comparable with diazepam⁵².



(46)

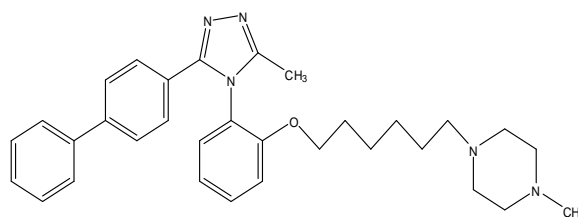
Carling RW et al. investigated that there is increasing evidence that compounds (**47**) with selectivity for gamma-aminobutyric acid-A (GABA-A) alpha2- and/ or alpha3-subtypes may retain the desirable anxiolytic activity of nonselective benzodiazepines but possess an improved side effect profile. In this study, they have described a novel series of GABA-A alpha2/alpha3 subtype- selective agonists leading to the identification of the non-sedating anxiolytic agents in preclinical animal assays⁵³.



(47)

Antihypertensive activity

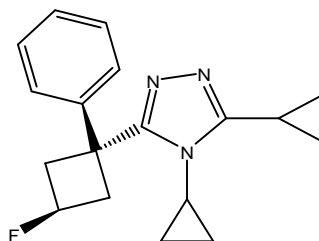
Kakefuda et al. Synthesized and evaluated a series of 5-(4-biphenyl) - 3-methyl-4-phenyl-1,2,4-triazole derivatives (**48**) as selective antagonists for human vasopressin V-1A receptor. The compounds were examined for their affinity to the cloned human V-1A receptor hV-1A and selectivity versus the cloned human V-2 receptor h-V2. One particular compound, 5-(4-biphenyl)-3-methyl-4-[2-[6-(4-methyl-1-piperazinyl) hexyloxy] phenyl]-1,2,4-triazole Showed potent affinity to hV-1A and high selectivity with a 1700-fold selectivity versus h-V2, it also showed antagonist activities toward an arginine vasopressin-induced increase in diastolic blood pressure after intravenous or oral administration and long-lasting oral activity⁵⁴.



(48)

Anti Dibetic activity

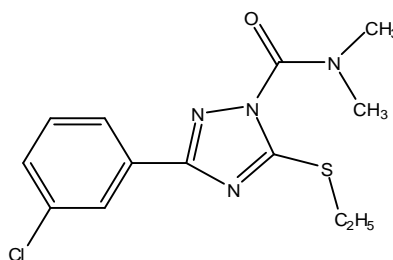
Zhu et al. demonstrated that 3-(phenylcyclobutyl)- 1,2,4-triazole derivatives (**49**) show reduction in the blood glucose and lipid levels by the inhibition of 11 - hydroxysteroid dehydrogenase type I (11 -HSDI)⁵⁵.



3,4-dicyclopropyl-5-(3-fluoro-1-phenylcyclobutyl)-4H-1,2,4-triazole

(49)

Ebdrup et al. studied four new classes of carbamoyltriazoles (**50**) to demonstrate the central role of the intracellular enzyme hormone-sensitive lipase (HSL) in regulating fatty acid metabolism for the treatment of insulin resistant and dyslipidemic disorders. On the basis of a lead structure from high throughput screening, they identified methyl-phenyl-carbamoyl-triazoles as potent and efficacious HSL inhibitors to show their antidiabetic activity⁵⁶.

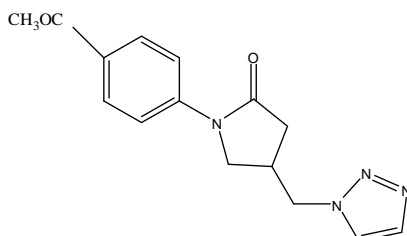


3-(3-chlorophenyl)-5-(ethylthio)-N,N-dimethyl-1H-1,2,4-triazole-1-carboxamide

(50)

Anti Bacterial Activity

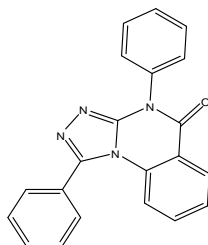
Demaray et al, The screening for antibacterial activity of C-5-substituted triazole-oxazolidinones (**51**) against *Mycobacterium smegmatis* ATCC 14468, *Bacillus subtilis* ATCC 6633, and *Enterococcus faecalis* ATCC 29212 was done by Demaray et al. Notably, the 3-(4-acetyl-phenyl)-5-(1H-1,2,3-triazol-1-yl)methyl-oxazolidin-2-one showed 4-fold lower MIC value than measure for isoniazid⁵⁷.



Chemical structure of 3-(4-acetyl-phenyl)-5-(1H-1,2,3-triazol-1-yl)methyl-oxazolidin-2-one

(51)

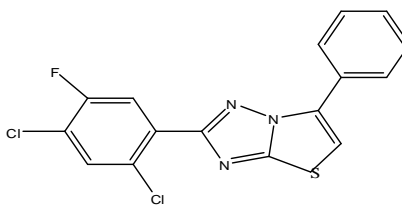
Pandey et al, synthesized a series of novel heterocyclic systems, viz. triazolo[4,3-a]-quinazolin-7-ones (**52**) [1,2,4,5]-tetrazino[4,3-a]-quinazolin-8-ones and indolo[2,3-c][1,2,4]-triazino[4,3-a]-quinazolin-8-ones and screened antibacterial activity against Gram-negative bacteria e.g. *Escherichia coli*, *Pseudomonas aeruginosa* and Gram-positive bacteria e.g. *Streptococcus pneumoniae*, *Bacillus subtilis*, as well as for antifungal activity against fungal stains such as *Candida albicans*, *Aspergillus fumigatus*, *Aspergillus flavus*, and *Aspergillus niger*. Some compounds showed potent antifungal and activity antibacterial⁵⁸.



(52)

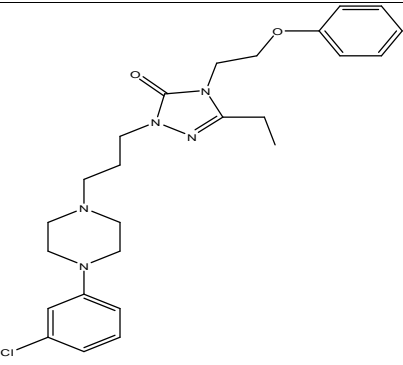
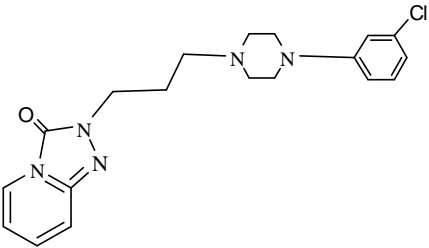
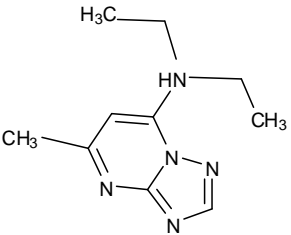
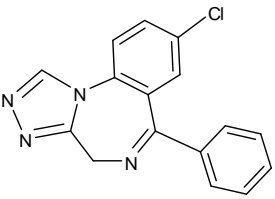
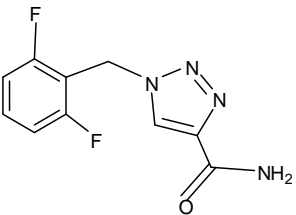
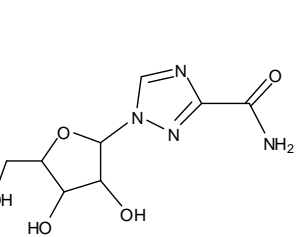
Chemical structure of triazolo[4,3-a]-quinazolin-7-one.

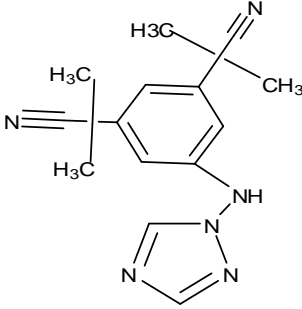
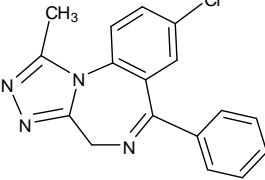
Karthikeyan synthesized a series of 2,4-dichloro-5-fluorophenyl bearing thiazolotriazoles (**53**) starting from 3-(2,4-dichloro-5-fluorophenyl)-4H-1,2,4-triazole-3-thiol. Some of the synthesized compounds were tested for their anti-inflammatory, analgesic and antimicrobial activities. Three compounds exhibited potent antibacterial activity whereas other compounds demonstrated significant antifungal activity⁵⁹.



(53)

Chemical structure of 2,4-dichloro-5-fluorophenyl bearing thiazolotriazole.

Nefazodone	Serzone		Antidepressant
Trazodone	Desyrel		Antidepressant
Trapidil	Trapiloid		Antihypertensive Vasodilator
Estazolam	Prosom		Sedative-Hypnotic
Rufinamide	Banzel		Antiepileptic
Ribavirin	Virazole		Antiviral

Anastrozole	Arimidex		Antineoplastic
Alprazolam	Xanax		(Tranquillizer)

References

1. Finar, I.L., "Organic Chemistry: Stereochemistry and the Chemistry of Natural Product, Vol.2, 5th Edition, pp 621.
2. Zech, B., Croetz, H. *J. Indian chem. Soc*, 1981, 280, 2923- 2926.
3. Gilchrist, T.L., *Heterocyclic Chemistry*. Singapore: Pearson Education India, 2005, 298–307.
4. Pellizzari, G. *Gazz. Chim. Ital*, 1911, 41, 20.
5. Atkinson MR, Polya J B, Triazoles. Part II. N-substitution of some 1: 2: 4-triazoles. *Journal of the Chemical Society*: 1954, 141.
6. Kwok SW, Fotsing J R, Fraser R J, Rodinov V O, Fokin VV, *Org Lett*, 2010, 12, 4217-4219.
7. Liu, P., Zhu, S., Xie, W., Synthesis and SAR studies of biaryloxysubstituted triazoles as antifungal agents. *Bioorg Med Chem Lett*, 2008, 18, 3261–3265.
8. Isloor, A.M., Kalluraya, B., Shetty, P., Regioselective reaction: synthesis, characterization and pharmacological studies of some new Mannich bases derived from 1,2,4-triazoles. *Eur J Med Chem*, 2009, 44, 3784–3787.
9. Shafiee, A., Sayadi, A., Roozbahani, M.H., Foroumadi, A., Kamal, F., Synthesis and *in vitro* antimicrobial evaluation of 5-(1-methyl-5-nitro-2-imidazolyl)-4H-1,2,4-triazoles. *Arch Pharm*, 2002, 335, 495-499.
10. Wuest, F., Tang, X., Kniess, T., Pietzsch, J., Suresh, M., Synthesis and cyclooxygenase inhibition of various (aryl-1,2,3-triazole-1-yl)-methane sulfonyl phenyl derivatives. *Bioorg Med Chem*, 2009, 17, 1146–1151.
11. Abdel-Rahman, Hussein, M.A., Synthesis of beta hydroxyl propanoic acid derivatives as potential anti-inflammatory, analgesic and antimicrobial agents. *Arch Pharm*, 2006, 339, 378–387.
12. Amir, M., Kumar, H., Javed, S.A., Khan, S.A., 1,3,4-Oxadiazole/ thiadiazole and 1,2,4-triazole derivatives of biphenyl- 4-yloxy acetic acid: Synthesis and preliminary evaluation of biological properties. *Eur J Med Chem*, 2008, 43, 2688-2698.
13. Mohamed, B.G., Abdel-Alim, A.A., Hussein, M.A., Synthesis of 1-acyl-2-alkylthio-1,2,4-triazolobenzimidazoles with antifungal, anti-inflammatory and analgesic effects. *Acta Pharm*, 2006, 56, 31-48.
14. Pattan Shasikant, et.al. Synthesis and evaluation of some novel 1,2,4-triazole derivatives for antimicrobial, antitubercular and anti-inflammatory activities. *Indian journal of chemistry*, 2012, 51B, 297-301.

15. Lin, R., Connolly, P.J., Huang, S., 1-Acyl-1H-[1,2,4]triazole-3,5-diamine analogues as novel and potent anticancer cyclin dependent kinase inhibitors: synthesis and evaluation of biological activities. *J Med Chem*, 2005, 48, 4208–4211.
16. El-Hawash, S.A., Habib, N.S., Kassem, M.A., Synthesis of some new quinoxalines for evaluation of in vitro antitumor and antimicrobial activities. *Arch Pharm*, 2006, 33, 564–571.
17. Pachuta-Stec, A., Rzymowska, J., Mazur, L., Mendyk, E., Pitucha, M., Rzaczy ska, Z., Synthesis, structure elucidation and antitumour activity of N-substituted amides of 3-(3-ethylthio-1,2,4-triazol-5-yl) propenoic acid. *Eur J Med Chem*, 2009, 44, 3788–3793.
18. Demirbas, N., Synthesis and antimicrobial activities of some new 1-(5-phenyl amino-[1,3,4] thiadiazol-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. *Eur J of Med Chem*, 2004, 39, 793–804.
19. Zhai, X., Zhao, Y.F., Liu, Y.J., Zhang, Y., Xun, F.Q., Liu, J., Gong, P., Synthesis and cytotoxicity studies of novel [1,2,4]triazolo[1,5-*a*]pyrimidine-7-amines. *Chem Pharm Bull*, 2008, 56, 941–945.
20. Ibrahim, D.A., Synthesis and biological evaluation of 3,6- disubstituted[1,2,4]triazolo[3,4-b] [1,3,4]thiadiazole derivatives as a novel class of potential anti tumor agents. *Eur J Med Chem*, 2009, 44, 2776–2781.
21. El-Hawash, S.A., Habib, N.S., Kassem, M.A., Synthesis of some new quinoxalines for evaluation of in vitro antitumor and antimicrobial activities. *Arch Pharm* 2006, 339, 564–571.
22. Mohamed, B.G., Abdel-Alim, A.A., Hussein, M.A., Synthesis of 1-acyl-2-alkylthio-1,2,4-triazolobenzimidazoles with antifungal, anti-inflammatory and analgesic effects. *Acta Pharm*, 2006, 56, 31–48.
23. Amir, M., Kumar, H., Javed, S.A., Khan, S.A., 1,3,4-Oxadiazole/ thiadiazole and 1,2,4-triazole derivatives of biphenyl- 4-yloxy acetic acid: Synthesis and preliminary evaluation of biological properties. *Eur J Med Chem*, 2008, 43, 2688-2698.
24. Sun, X. Y., Jin, Y. Z., Li, F. N., Li, G., Chai, K. Y., and Quan, Z. S., Synthesis of 8-alkoxy-4,5-dihydro-[1,2,4]triazole [4,3-*a*]quinoline-1-ones and evaluation of their anticonvulsant properties. *Arch Pharm Res*, 2006, 29, 1080–1085.
25. Pandeya, S.N., Sriram, D., Yogeewari, P., Stables, J.P., Anticonvulsants and neurotoxicity evaluation of 5-(un)-substituted isatinimino derivatives. *Pharmazie*, 2001, 56, 875.
26. Karakurt, A., Aytemir, M.D., Stables, J.P., Ozalp, M., Betul, F. Kaynak., Ozbey, S., Dalkara, S., Synthesis of Some Oxime Ether Derivatives of 1-(2-Naphthyl)-2-(1,2,4-triazol-1-yl)ethanone and Their Anticonvulsant and Antimicrobial Activities. *Arch Pharm*, 2006, 339, 513–520.
27. Siddiqui, N., Alam, M.S., Ahsan, W., Synthesis, anticonvulsant and toxicity evaluation of 2-(1*H*-indol-3-yl)acetyl-N-(substituted phenyl)hydrazine carbothioamides and their related heterocyclic derivatives. *Acta Pharm*, 2008, 58, 445–454.
28. Pandeya, S.N., Laxmi, B.S., Pandey, A., Biological Activity of Mannich Bases. *Ind J Pharm Sci*, 2003, 65(3), 213-222.
29. Husain, M.I., Amir M., Singh, E., Synthesis and anti-tubercular activities of [5-(2 furyl)-1,2,4-triazoles-3yl thio] acehydrazide derivatives. *Indian J Chem*, 1987, 26B, 2512-54.
30. Rahimani, M.A., Kalluraya, B., Synthesis, Characterization, Antimicrobial and Anthelmintic Activity of some Sydnone-N-Mannich Bases. *J Ind Council Chem*, 2008, 25(1), 10-14.
31. Kharb, R., Sharma, P.C., Bhandari, A., Shaharyar, M., Synthesis, spectral characterization and anthelmintic evaluation of some novel imidazole bearing triazole derivatives. *Der Pharmacia Lettr*, 2012, 4, 652-657.
32. Vishnumurthy, K.A., Satyendra RV, Vagdevi HM, Rajesh KP, Manjunatha H, Shruthi A, Synthesis, in vitro antioxidant, anthelmintic and molecular docking studies of novel dichloro substituted benzoxazole- triazolo-thione derivatives. *European Journal of Medicinal Chemistry*, 2011, 46, 3078–3084.
33. Wang, Z., Wu, B., Kuhen, K.L., Bursulaya, B., Nguyen, T.N., Nguyen, D.G., He Y., Synthesis and biological evaluations of sulfanyltriazoles as novel HIV-1 non-nucleoside reverse transcriptase inhibitors. *Bioorg Med Chem Lett*, 2006, 16, 4174–4177.

34. De La Rosa, M., et.al, Trisubstituted triazoles as potent non-nucleoside inhibitors of HIV-1 reverse transcriptase. *Bioorg Med Chem Lett*, 2006, 16, 4444–4449.
35. Jordao, A.K., Afonso, P.P., Ferreira, V.F., De Souza, M.C., Almeida, M.C., Beltrame, C.O., Paiva, D.P., Wardell, S.M., Wardell, J.L., Tiekink, E.R., Damaso, C.R., Cunha, AC. Antiviral evaluation of N-amino-1,2,3- triazoles against Cantagalo virus replication in cell culture. *Eur J Med Chem*, 2009, 44, 3777–3783.
36. Chan, D. C., Laughton, C.A., Queener, S. F., Stevens, S.F., Structural studies on bioactive compounds. Part 36: design, synthesis and biological evaluation of pyrimethamine-based antifolates against *Pneumocystis carinii*. *Bioorg Med Chem*, 2002, 10, 3001-3010.
37. Mishra, N., Arora, P., Kumar, B., Mishra, L.C., Bhattacharya, A., Awasthi, S.K., Bhasin, V.K., Synthesis of novel substituted 1,3-diaryl propenone derivatives and their antimalarial activity in vitro. *Eur J Med Chem*, 2008, 43, 1530-1535.
38. Gujjar, R., Marwaha, A., et.al. Synthesis of novel substituted 1,3-diaryl propenone derivatives and their antimalarial activity in vitro. *J Med Chem*, 2009, 52, 1864-1872.
39. Havaldar, F.H., Patil, A.R., Syntheses of 1, 2, 4 Triazole Derivatives and their Biological Activity. *Eur J Chem*, 2008, 5, 347-354.
40. Shafiee, A., Sayadi, A., Roozbahani, M.H., Foroumadi, A., Kamal, F., Synthesis and in vitro Antimicrobial Evaluation of 5-(1-Methyl-5-nitro-2- imidazolyl)-4H-1,2,4-triazoles . *Arch Pharm*, 2002, 335, 495-499.
41. Havaldar, F.H., Patil, A.R., Syntheses of 1, 2, 4 Triazole Derivatives and their Biological Activity. *Eur J Med Chem*, 2008, 5, 347-354.
42. Kokil, R.G., Synthesis and In Vitro Evaluation of Novel 1, 2, 4-Triazole Derivatives as Antifungal Agents. *Letters in drug Design & Discovery*, 2010, 7, 46-49.
43. Siddiqui, A. A., Arora, Amit., Synthesis of some 1,2,4-triazoles as potential antifungal agents. *Indian journal of chemistry*, 2005, 44 B, 838.
44. Shiradkar, M., Kumar, Suresh., Dasari, V., Tatikonda, S., Akula, K.C., Shah, R., Clubbed triazoles: a novel approach to antitubercular drugs. *Eur J Med Chem*, 2007, 42, 807–816.
45. Polya, J.B., *Comprehensive Heterocyclic Chemistry*, 1984: vol 5, Pergamon Press, P-733.
46. Kaplancikli, T.A., Turan-Zitouni, G., Chevallet, P. Synthesis and antituberculosis activity of new 3-alkylsulfanyl-1,2,4-triazole derivatives. *J Enzyme Inhib Med Chem*, 2005, 20,179–182.
47. Upadhayaya, R.S., Kulkarni, G.M., Vasireddy, N.R., Vandavasi, J.K., Dixit, S.S., Sharma, V., Chattopadhyaya, J., Design, synthesis and biological evaluation of novel triazole, urea and thiourea derivatives of quinoline against *Mycobacterium tuberculosis*. *Bioorg Med Chem*, 2009, 17, 4681–4692.
48. Jadhav, G.R., Shaikh, M.U., Kale, R.P., Shiradkar, M.R., Gill, C.H., SAR study of clubbed [1,2,4]-triazolyl with fluorobenzimidazoles as antimicrobial and antituberculosis agents. *Eur J Med Chem*, 2009, 44, 2930–2935.
49. Zhu, Y., et al. Phenylcyclobutyl triazoles as selective inhibitors of 11beta-hydroxysteroid dehydrogenase type I. *Bioorg Med Chem Lett*, 2008, 18, 3412–3416.
50. Ebdrup, S., Sorensen, L.G., Olsen, O.H., Jacobsen, P., Synthesis and structure-activity relationship for a novel class of potent and selective carbamoyl-triazole based inhibitors of hormone sensitive lipase. *J Med Chem*, 2004, 47, 400–410.
51. Carling, R.W., et al, 3-phenyl-6-(2-pyridyl)methoxy-1,2,4-triazolo[3,4-a]phthalazines and analogues: high-affinity gamma-amino butyric acid-A benzodiazepine receptor ligands with alpha 2, alpha 3, and alpha 5-subtype binding selectivity over alpha 1. *J Med Chem*, 2004, 47, 1807–1822.
52. Akbarzadeh, Tabatabai, S.A., Khoshnoud, M.J., Shafaghi, B., Shafiee, A., Design and synthesis of 4H-3-(2-phenoxy) phenyl-1,2,4-triazole derivatives as benzodiazepine receptor agonists. *Bioorg Med Chem*, 2003, 11, 769–773.
53. Carling, R.W., et.al, a functionally selective gamma-aminobutyric acid (A) (GABA (A)) alpha2/alpha3-subtype selective agonist that exhibits potent anxiolytic activity. *J Med Chem*, 2005, 48, 7089–7092.
54. Kakefuda, A., Suzuki, T., Tobe, T., Tsukada, J., Tahara, A., Sakamoto, S., Tsukamoto, S., Synthesis and pharmacological evaluation of 5-(4-biphenyl)-3-methyl-4-phenyl-1,2,4-triazole derivatives as a

- novel class of selective antagonists for the human vasopressin V(1A) receptor. *J Med Chem*, 2002, 45, 2589–2598.
55. Zhu, Y., Olson, S.H., Graham, D., Phenylcyclobutyl triazoles as selective inhibitors of 11 - hydroxysteroid dehydrogenase type. *Bioorg Med Chem Lett*, 2008, 18, 3412–3416.
 56. Ebdrup. S., Sorensen, L.G., Olsen, O.H., Jacobsen, P. Synthesis and structure–activity relationship for a novel class of potent and selective carbamoyl-triazole based inhibitors of hormone sensitive lipase. *J Med Chem*, 2004, 47, 400–410.
 57. Demaray, J.A., Thuener, J.E., Dawson MN, Sucheck SJ, Synthesis of triazole-oxazolidinones via a one-pot reaction and evaluation of their antimicrobial activity. *Bioorg Med Chem Lett*, 2008, 18, 4868–48.
 58. Pandey, S.K., Singh, A., Nizamuddin, A., Antimicrobial studies of some novel quinazolinones fused with [1,2,4]-triazole, [1,2,4]-triazine and [1,2,4,5]- tetrazine rings. *Eur J Med Chem*, 2009, 44, 1188–1197.
 59. Karthikeyan, M.S., Synthesis, analgesic, anti-inflammatory and antimicrobial studies of 2,4-dichloro-5-fluorophenyl containing thiazolotriazoles. *Eur J Med Chem*, 2009, 44, 827–833.
 60. Kim, James. Tang, Jean. Y., Gong, Ruoyu, Kim., Jynho, Lee., John, J., Clemons, Karl, V., Chong, Curtis. R., Chang, Kris. S., et al. Itraconazole, a Commonly Used Antifungal that Inhibits Hedgehog Pathway Activity and Cancer Growth. *Cancer Cell* 2010, 17 (4), 388–99.
 61. Agarwal, R., Singh, N., Amphotericin B is still the drug of choice for invasive aspergillosis. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. *Am J Respir Crit Care Med*, 2006, 174 (1), 102.
 62. Kragie, Laura, Turner, Stephanie. D., Patten, Christopher. J., Crespi, Charles. L., Stresse, David. M. Assessing Pregnancy Risks of Azole Antifungals Using a High Throughput Aromatase Inhibition Assay. *Endocrine Research*, 2002, 28 (3), 129–40.
 63. Raad, I., Hachem, R., Herbrecht, R., et al., Posaconazole as salvage treatment for invasive fusariosis in patients with underlying hematologic malignancy and other conditions. *Clin Infect Dis*, 2006, 42 (10), 1398–1403.
 64. <http://en.wikipedia.org/wiki/Rilmazafone>.
 65. Sussman, N., Ginsberg, D.L., Bikoff, J. Effects of nefazodone on body weight: a pooled analysis of selective serotonin reuptake inhibitor- and imipramine-controlled trials. *The Journal of Clinical Psychiatry*, 2001, 62 (4), 256–60.
 66. Nierenberg, A.A., Adler, L.A., Peselow, E., Zornberg, G., Rosenthal, M.. Trazodone for antidepressant-associated insomnia. *Am J Psychiatry*, 1994, 151 (7), 1069–72.
 67. <http://en.wikipedia.org/wiki/Trapidil>.
 68. Akbarzadeh, T., Tabatabai, S.A., Khoshnoud, M.J., Shafaghi, B., Shafiee, A., Design and synthesis of 4H-3-(2-phenoxy)phenyl-1,2,4-triazole derivatives as benzodiazepine receptor agonists. *Bioorg. Med. Chem*, 2003, 11 (5), 769–73.
 69. Brodie, M.J., Rosenfeld, W.E., Vazquez, B., Sachdeo, R., Perdomo, C., Mann, A., Arroyo, S., Rufinamide for the adjunctive treatment of partial seizures in adults and adolescents: a randomized placebo-controlled trial. *Epilepsia*, 2009, 50 (8), 1899–909.
 70. Sidwell, R.W., Bailey, K.W., Wong, M.H., Barnard, D.L., Smee, D.F., In vitro and in vivo influenza virus-inhibitory effects of viraclidine. *Antiviral Res.*, 2005, 68 (1), 10–17.
 71. Murras, N., Bishop, K., Merinbaum, D., Emeribe, U., Agbo, F., Lowe, E., Pharmacokinetics and pharmacodynamics of anastrozole in pubertal boys with recent-onset gynecomastia. *J. Clin. Endocrinol. Metab*, 2009, 94 (8), 2975–8.
 72. Sheehan, D.V., Sheehan, K.H., Raj, B.A., The Speed of Onset of Action of Alprazolam-XR Compared to Alprazolam-CT in Panic Disorder". *Psychopharmacology Bulletin*, 2007, 40 (2), 63–81.

Triazole as Pharmaceuticals Potentials

**Rakesh Kumar^{1*}, Mohd. Shahar Yar²,
Saurabh Chaturvedi³, Atul Srivastava³.**

***Corres. Author: rakeshpsit.saini@gmail.com**

Mob.no. 09452075670

★★★★★