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Review Article

A Short review on 1, 2, 4-Triazole with various pharmacological activity

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Heterocyclic compounds have been an interesting area for the study of synthesis and biological activity of novel 1, 2, 4-Triazole derivatives for a long time. Heterocyclic compounds possess diverse biological properties that have led to intense study and research of these compounds. One of these compounds 1, 2, 4-Triazole is a versatile heterocyclic nucleus is a novel molecule which attract the medicinal chemist to search a new therapeutic molecule. 1,2,4-Triazole exhibited a wide range of biological activities which includes anti-bacterial, anti-fungal, anticonvulsant, analgesic, anti-depressent, anti-cancer, antioxidant, anti-microbial, anti-inflammatory and anti-malarial activities. Results of various derivatives of different Triazole and their substitutions with diverse biological activities are reviewed in present article.

Keywords: *Heterocyclic compounds, 1, 2, 4-Triazole Derivatives, Biological activities.*

Introduction of 1, 2, 4-triazole-

There is significant and continuous concern in the chemistry of five-member N-heterocycle compounds, mainly tetrazole (CH_2N_4), triazoles ($C_2H_3N_3$), and their substituted derivatives. Triazole exists as two isomers, 1,2,3-triazoles and 1,2,4-triazoles, as shown in (Fig. 1). [1]

Figure no. 1- Isomers of Triazole

A large number of 1,2,4-triazole, a heterocyclic derivative exhibits important structural fragments and considered as biologically active compounds such as antifungal, anticonvulsant anti-tubercular, antioxidant, anti-inflammatory inhibition, anticancer, and antimicrobial activity, [2-7] corrosion inhibitors, [8] pesticides, [9] dyes, [10] acid-base indicator, [11] and other industrial chemicals [12]. At 1885, Bladin was the first scientist who gave the name of (triazole) to the carbon nitrogen ring system ($C_2N_3H_3$) and described triazoles derivatives. [13].

Biological Activities of 1, 2, 4-Triazoles-

The synthesized compounds will be screened for following biological activities-

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a. Antibacterial activity:

Synthesized triazole substituted triazolo-pyrimidine derivatives and found to possess antibacterial activity {R= pyridyl}. [14]

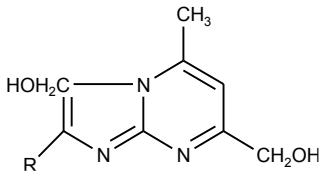

Figure no. 2

b. Antifungal Activity:

Reported a novel 2-substituted-5-[isopropylthiazole] clubbed 1,2,4-triazole were synthesized as potent antifungal agent. The activity was shown by the compound named as 3-(4-Isopropylthiazol-2-yl)-6-(4-nitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazole. [15]

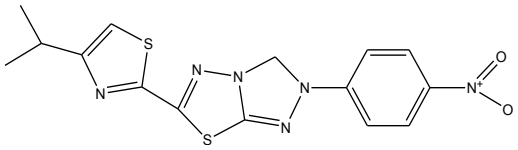

Figure no. 3

c. Anti-inflammatory activity:

Reported a series of 3-(methyl/ethyl sulfonyl)-5-aryl-1,2,4-triazole from 5-aryl-3-mercapto-1,2,4-triazole and screened them for their antiinflammatory and analgesic activity. Results shows that compounds having an alkylsulfone derivative were greater active than those of alkylthio group. [16]

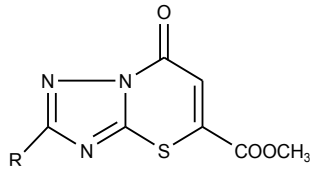

Figure no. 4

Synthesized a series of 1-acyl-3-phenyl-5-alkyltriazoles, and evaluated these derivatives for anti-inflammatory activity using the mouse active Arthus (MAA) reaction as the test system. Modification of the acyl group, 4-phenyl substituent, and alkyl group led to the selection of the most active member of this series, 1-acetyl-3-(4-chlorophenyl)-5-methyl-1,2,4-triazole. [17]

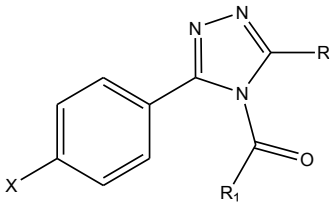

Figure no. 5

Synthesized a series of 3-[1-(4-(2-methylpropyl) phenyl) ethyl]-1, 2, 4-triazole-5-thione derivatives and evaluated their anti-inflammatory activity in gastric ulceration studies the synthesized compounds were generally found to be safe at a 200 mg/kg dose level. [18]

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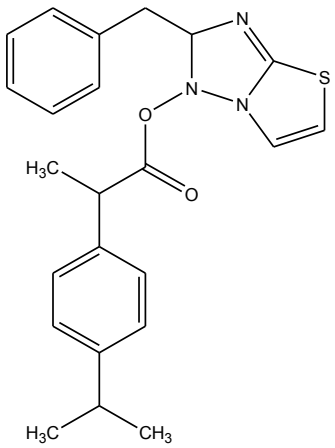


Figure no. 6

d. Analgesic activity:

Reported a synthesis of 3-substituted-4-(3-disubstituted-1-triazenyl)-4H-1,2,4-triazol-5-thiol and these compounds were evaluated for their analgesic activity. Some of the compounds showed excellent analgesic activity. [19]

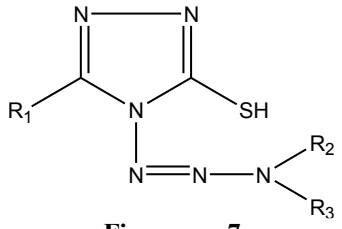


Figure no. 7

e. Anticonvulsant activity:

Designed and synthesized the substituted N-(5-mercapto-3-pyridyl-3-yl-4H-1,2,4-triazol-4-yl)-thiosemicarbazone from nicotinic acid and evaluated them for anticonvulsant activity by Maximum Electroshock (MES) method and found that total recovery time and time for hind limb extension recovery for compound was less than the standard (Phenytoin). [20]

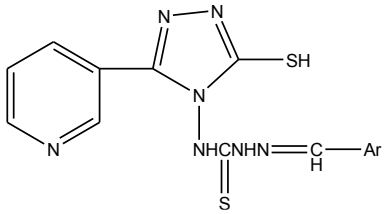


Figure no. 8

Synthesized a series of New-substituted Mercapto-triazoles and thiazolidiones derivatives and evaluated their MAO Inhibitory and anticonvulsant activity. [21]

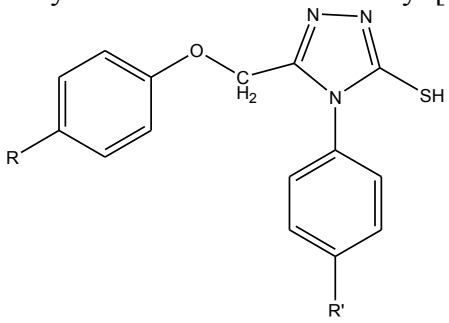


Figure no. 9

Synthesized a series of 3-[4-(substituted phenyl)-1,3-thiazol-2-ylamino]-4-(substituted phenyl)-4,5-dihydro-1H-1,2,4-triazole-5-thiones by clubbing thiazole and triazole moieties, keeping in view the structural requirement for the pharmacophore model for anticonvulsant activity. Two compounds c1 and c2 showed significant anticonvulsant activity in both MES and subcutaneous pentylenetetrazole (sc PTZ) screenings along with good safety margin. [22]

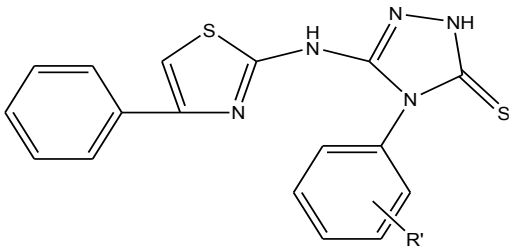
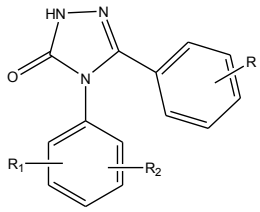


Figure no. 10

Synthesized a new series of 4,5-diphenyl-2H-1,2,4-triazol-3(4H)-one, all the compounds were evaluated for their anticonvulsant activity in four animal models of seizures, i.e. maximal electroshock seizure (MES), subcutaneous pentylenetetrazole (sc PTZ), subcutaneous strychnine (sc STY), and subcutaneous picrotoxin (sc PIC)-induced seizure threshold tests. The compounds were also evaluated for neurotoxicity. [23]



R = H, NO2, NH3, CH3

R1= H, 2-CH3

R2= 4-CH3, 5-CH3

Figure no. 11

Synthesized a series of Novel 8-chloro-6-(2-fluorophenyl)-1-(aryl)-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepines by treating 7-chloro-5-(2-fluorophenyl)-1,3-dihydro-2H-1,4-benzodiazepine-2-thione with various aromatic acid hydrazides. Compounds were tested for anticonvulsant activity. Four of the tested compounds exhibited excellent anticonvulsant activity in

comparison with standard drug, diazepam. [24]

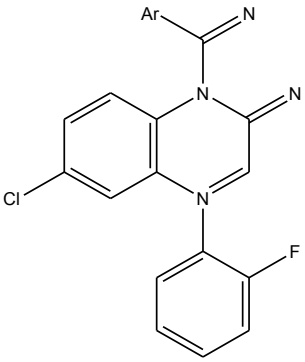


Figure no. 12

A series of 4-(4-alkoxylphenyl)-3-ethyl-4H-1,2,4-triazole derivatives where synthesized as open-chain analogues of 7-alkoxyl-4,5-dihydro[1,2,4]triazolo[4,3-a]quinolines.
Their anticonvulsant activities were evaluated by the maximal electroshock test and their neurotoxicity was evaluated by the rotarod neurotoxicity test. [25]

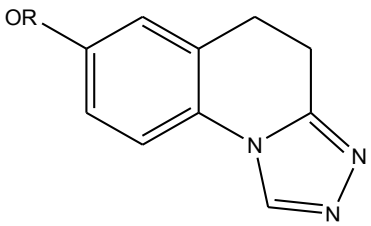


Figure no. 13

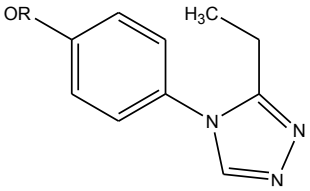
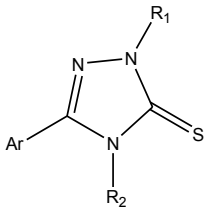


Figure no. 14

f. Antidepressant activity:
Synthesized a series of 5-aryl-1,2,4-triazole-3H-1,2,4-triazole-3-thiones More active member of this series were substituted by haloaryl groups at position 5 of the triazole nucleus and by methyl group at position 2 and 4 position. Several member of this series were potent antagonist of reserpine induced ptosis in mice. [26]



Ar = C_6H_5, R_2 =CH_3

Figure no. 15

Synthesized a series of triazole-pyrazoline derivatives and screened them using both modified forced swimming and tail suspension test. Rota-rod test was also performed for the examination of probable neurological deficits due to the test compounds. Compounds k-a and k-b were more effective than the reference drug fluoxetine with respect to anti depressant activity. [27]

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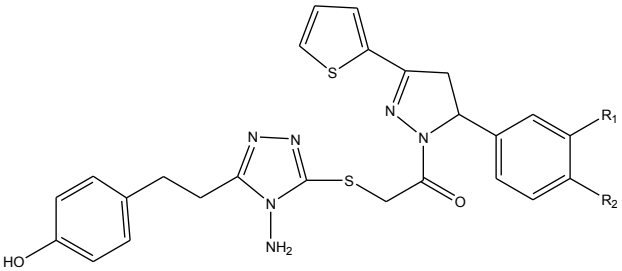


Figure no. 16

g. Antimicrobial activity:
Synthesized a series of Schiff bases of Triazole which show antibacterial as well as antifungal activity. 5-phenyl, 4-(substituted) amino, 3-mercapto 1,2,4-triazoles show anti-microbial activity. [28]

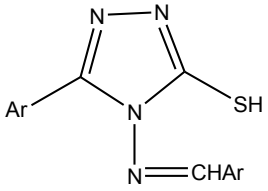
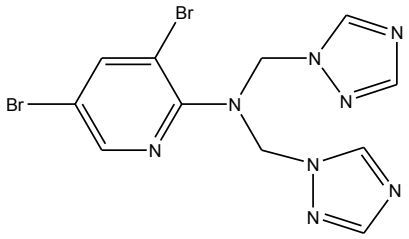


Figure no. 17

Synthesized a series of six new N,N-bis(1,2,4-triazole-1-ylmethyl)amine, in one step condensation of 1-(hydroxymethyl) with different amines and their compounds were evaluated for their antifungal activity against the budding yeast Saccharomyces cerevisiae and their antibacterial activity against Escherichia coli fallowing derivatives was found most active. [29]



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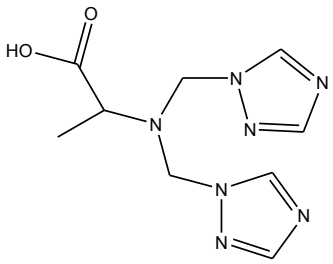

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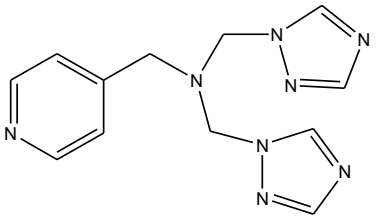

Figure no. 20

h. Antioxidant activity:

Damage to cells caused by free radical is supposed to play an essential role in the aging process and in disease development. antioxidants are our first line of protection against free radical damage, The antioxidants became even more critical with amplified exposure to free radicals. pollution, cigarette smoke, drugs, illness, stress and even exercise can increase free radical exposure. [30]

Synthesized and evaluated antioxidant activity of 4-amino-5-phenyl-4H-1,2,4-triazole-3-thiol derivatives (21). [31]

Found that tri-substituted triazole (22) and (23) possess highly potent antioxidant properties. [32]

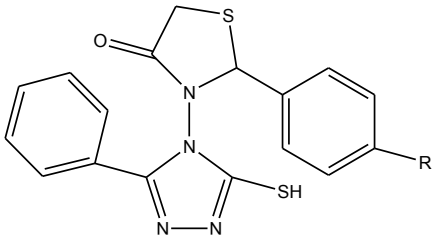

Figure no. 21

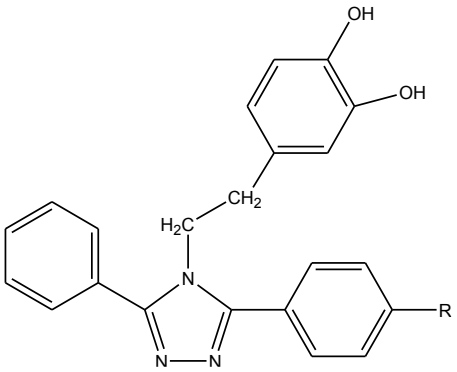

Figure no. 22

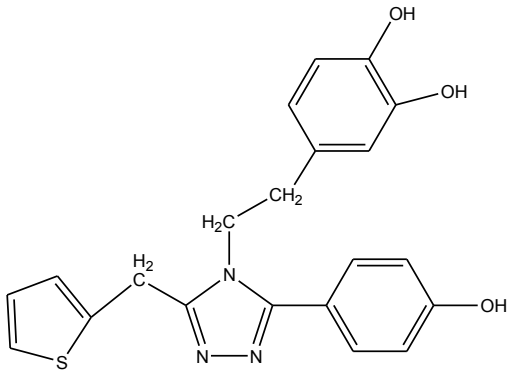

Figure no. 23

i. Anticancer activity:

Synthesized a series of heterocyclic-fused 1,2,3 by 1,3-dipolar cycloaddition of heterocyclic ketene aminals or N, O-acetals with sodium azide and polyhalo isopthalonitriles and evaluated in vitro against a panel of human tumour cell lines. Compound 4-Methoxy-phenyl substituted 1,3,-oxazoheterocycle fused 1,2,3 triazole was found to be the most potent derivative against A 431 and K 562 human tumor cell lines. [33]

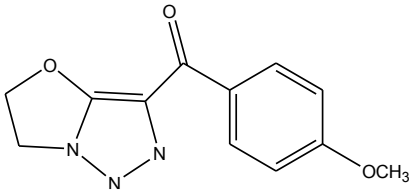

Figure no. 24

Synthesized a series of 3-unsubstituted and 3-substituted 7-aryl-5H-6,7-dihydroimidazo[2,1-c]1,2,4-triazoles derivatives and evaluated there anticancer activity. Compound H was found to be the most effective in vitro against human colon adenocarcinoma cell line (LS180). [34]

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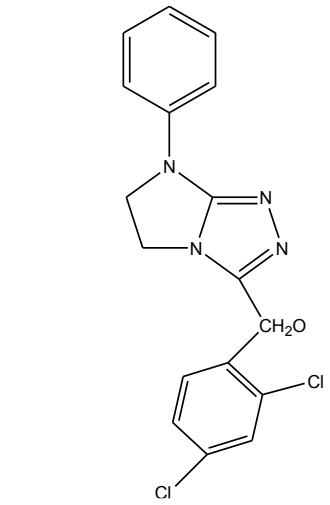

Figure no. 25

j. Antimalarial activity:

Synthesized a series of triazole-linked chalcone and dienone hybrid compounds and evaluated there antimalarial activity Several chalcone-chloroquinoline hybrid compounds were found to be notably active, with compound, the most active, exhibiting submicromolar IC-50 values against the D-10, Dd-2 and W-2 strains of Plasmodium falciparum. [35]

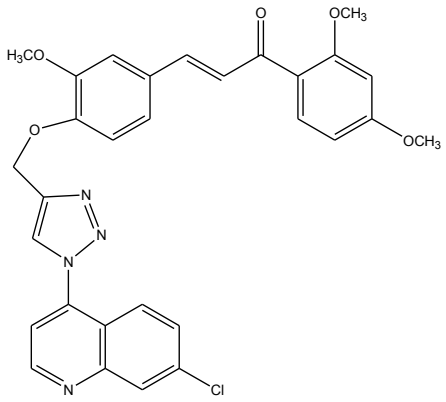

Figure no. 26

Conclusion

New synthetic strategies. Furthermore biological activity with new dimension need to be explored for 1,2,4-Triazole. Therefore

this review may be helpful for medicinal chemist.

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