International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

# A Comprehensive review on 1, 2,4 Triazole.

Pravin B. Jadhav[1], Amol M. Shirode, Sandip B. Ahire, Vinod A. Bairagi
*1, 2, 3 Assistant Professor, K.B.H.S.S. Trust's Institute of Pharmacy, Malegaon Dist: Nashik, 423105, Maharashtra, India.*
*4, Professor, K.B.H.S.S. Trust's Institute of Pharmacy, Malegaon Dist: Nashik, 423105, Maharashtra, India.*
**Corresponding author: Email: pravinb.jadhav24@gmail.com*

Date Of Submission: 05-05-2021 Date Of Acceptance: 22-05-2021

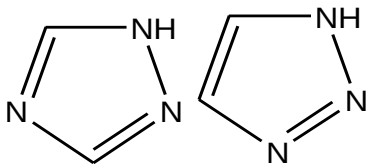
**ABSTRACT:** The 1, 2, 4-triazole ring is wide-ranging essential structural features of many synthetic compounds with extended therapeutic efficacy. Since form last many years, heterocyclic compounds have been explored comprehensively owing to their remarkable biological activities.
Theextended pharmacological activity and therapeutic efficacy has attracted the attention of many researchers to recognize the skeleton for its wide potential.In last few decades,antimicrobial activities, anti-cancer, antiviral, anti-inflammatory, anti-fertility, anti-tubercular activity andanti-corrosion properties of substituted triazoles have been reported**.**Basic focus has been specified to structure-activity relationship, pharmacological activities of various mono as well as poly substituted triazolesto explorethis heterocyclic ring in the field ofmedicinal chemistry.
The introduction of various 1, 2, 4, triazoles derivatives with their diversified pharmacological effects hasbeen reported. 1, 2, 4,-triazole and its derivatives attributes its valuable importance in the health sectors with biological actions like the antineoplastic, antifungal and antibacterial effects.
In this review we have summarizes several development during the past some decades in medicinal chemistry of 1, 2, 4 triazole derivatives with pharmacological activities. 1, 2, 4-triazole scaffold owning broad spectrum of pharmacological activities are extensively discussed.

**Keywords:**1, 2, 4 - Triazoles, Heterocycles, Antifungal, Antineoplastic, Antibacterial,Structure Activity Relationship.

## I. INTRODUCTION:

The chemistry and rational design of 1, 2, 4- triazoles and their fused heterocyclic derivatives have attractedsignificantattentiontowards their effective structural and biological importance. 1, 2, 4- triazolescaffold has been covered a wide variety of medicinallyactive drug candidates including antifungal, antibacterial, analgesics and anti-inflammatory, antineoplastic, antiviral, sedatives, anxiolytics, anti-convulsants, antimigraine, antihistaminic, CNS stimulants and other activities.[1]Thus 1,2,4 triazole units have fascinatedsignificant attention in fields, such as pharmaceuticals and agrochemical research also in the material sciences due to their distinctive structure and biological properties.[2]

**Triazole:**
Triazole is a heterocyclic compound containing 5 membered unsaturated ring structure composed of 3 nitrogen atom and 2 carbon atom. There are two isomer of triazole i.e. 1,2,3 triazole& 1,2,4triazole.



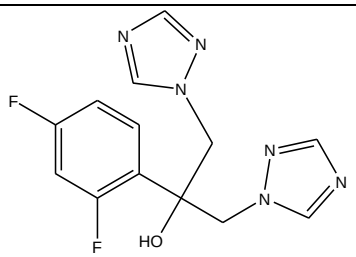
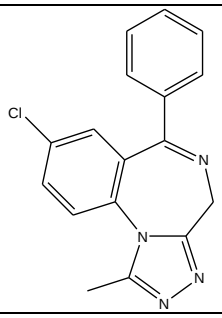
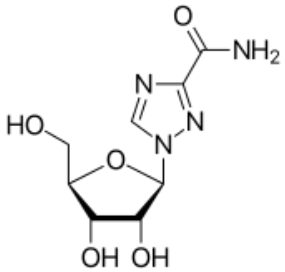
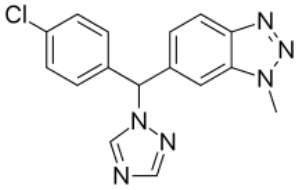
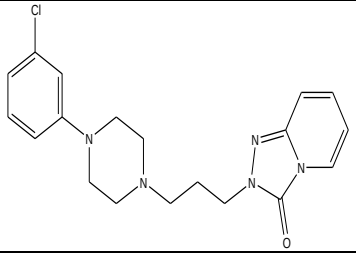

**1,2,4 triazole** **1,2,3 triazole**

Five-membered nitrogen heterocyclic compounds are important structural fragments and considered as biologically active compounds corrosion inhibitors, pesticides, dyes, acid-base indicator, and other industrial chemicals. At 1885, Bladin was the first science who gave the name of (triazole) to the carbon nitrogen ring system ($C_2N_3H_3$) and described triazolesderivatives.[3]Triazole also known as Pyrrodiazole.

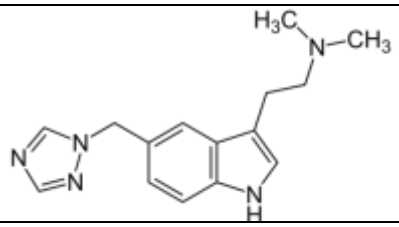
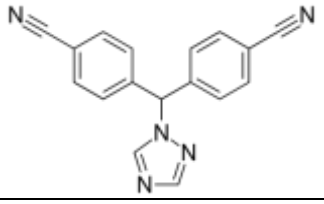
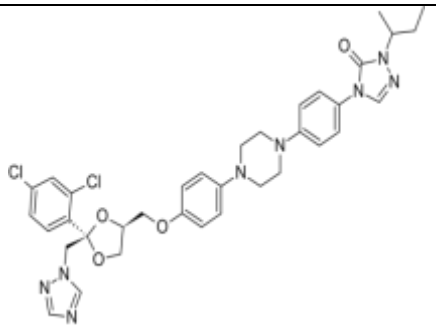
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

**Clinically used 1, 2, 4-triazole containing drugs:**
1,2,4-Triazole and its derivatives possess widely differing activities e.g. antibacterial, antifungal, anticancer, antituberculer, anti-inflammatory, analgesic, antiviral, anti-nociceptive, anti-convulsant, anti-corrosive, anthelmintic, antioxidant, urease & lipase inhibitors, hypoglycaemic,anti-migraine, anti-proliferative, sedative, diuretic, muscle relaxant and anti- HIV 50.[4]

**Table No: 1, clinically used 1, 2, 4-triazole containing drugs**

| No. | Drug | Structure | Use/Category |
|---|---|---|---|
| 1 | Fluconazole |  | Antifungal |
| 2 | Alprazolam |  | Anxiolytic, Hypnotic, Sedative**.** |
| 3 | Ribavirin |  | Antiviral |
| 4 | Vorozole |  | Aromatase Inhibitor, Antineoplastic |
| 5 | Trazodone |  | Antidepressant |

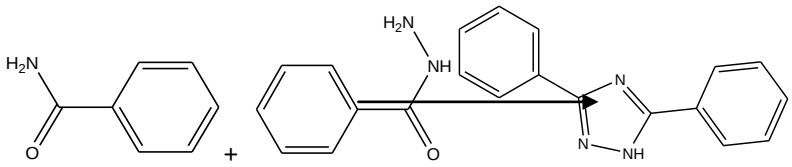
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

| | | | |
|---|---|---|---|
| 6 | Rizatriptan |  | Ant migraine |
| 7 | Letrozole |  | Breast Cancer |
| 8 | Itraconazole |  | Antifungal |

**Methods of Synthesis:**

**Pellizzari reaction:**

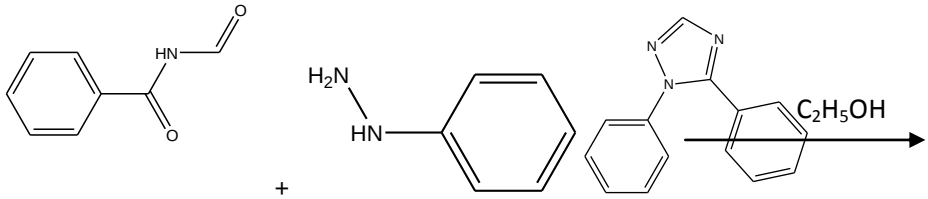
Heating the mixture of amide and acyl hydrazide has been made 1, 2, 4-triazole derivative is known as Pellizzari reaction. This method hasbeen described that the mixture of formamide and hydrazine hydrochloride heated with KOH yield of 1, 2, 4-triazole. For example benzamide and benzoyl hydrazideyields 3,5-diphenyl-1,2,4-triazole.[4]



Benzamidebenzoyl hydrazide3,5-diphenyl-1,2,4-triazole

**Einhorn – Brunner Reaction:**

The Einhorn–Brunner reaction is the condensation between hydrazines or mono substituted hydrazine and diacylamines in the presence of weak acid to form 1, 2 4-triazole. For example: N-formylbenzamide andphenyl hydrazine gave 1, 5-diphenyl- 1,2,4-triazole. [4]



N-formylbenzamidephenyl hydrazine 1,5-diohenyl- 1, 2,4-triazole

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

**Chemistry of 1, 2, 4-triazole:**

**Chemical properties**

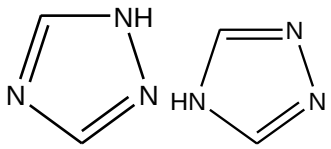
- Molecular formula - $C_2H_3N_3$
- Molecular weight - 69gm/mol
- Solublity- Soluble in water
- Melting point - 393 to 394 K
- Boiling point - 500 to 533 K

**Aromaticity and Resonance Effect:**

Stability of triazole ring is described by aromaticity. The donation of the one π electron from each atom connected by double bonds, also involvement of the three nitrogen atom and two carbon atom has been formed an aromatic sextet. [35]In addition to this triazolescaffold is stabilized by resonance also known as tautomeric forms.[4]

**Tautomerism in 1, 2, 4 –Triazole:**

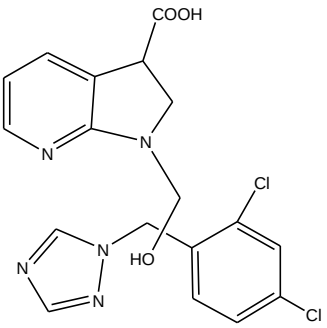
- There are two tautomeric forms of 1,2,4 – triazole i.e. 1H-1,2,4-triazole(a) and 4H-1,2,4 – triazole(b).
- According to various studies form a is more stable than form b.



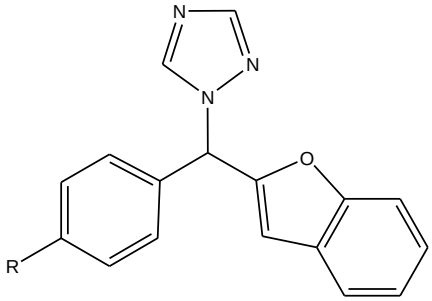

ab

**II. Rational Design Approaches (Structure Activity Relationships of 1, 2, 4, -triazole):**

**1, 2, 4–Triazole (1-Substituted):**




**(1)**




2

The compound(1)exhibited high biological activity against Candida albicans, Candida parapsilosis and Candida krusei as compared to medicinal agent fluconazole, while it has higher activity against Torulopsisglabrata than fluconazole. It has been noted that this compound recognized higher activities against C. parapsilosis than fluconazole.[5]

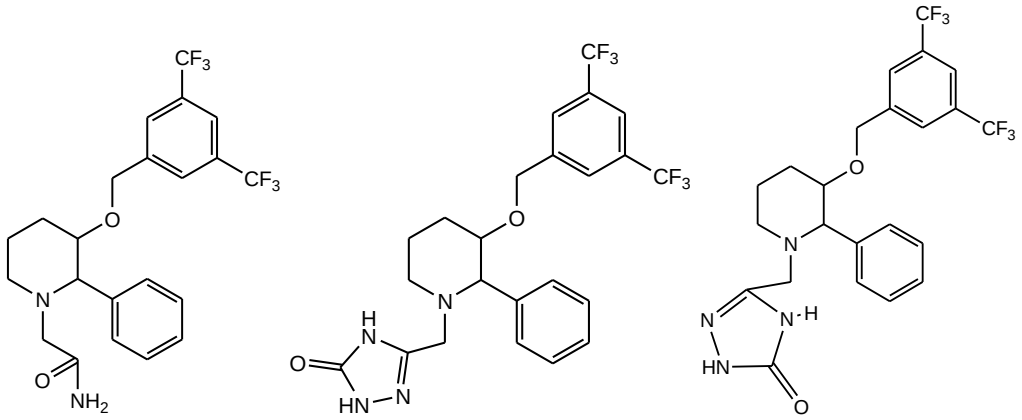
R=Alkyl/Aryl

A series of 4-alkyl/aryl substituted-1-[benzofuran-2-yl-phenylmethyl]-1Htriazoles(2) was synthesized

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

and screened for their inhibitory activity against CYP26A1 (IC504.5 and 7 μM respectively, using a MCF-7 cell based assay by Pautus et al.[6]

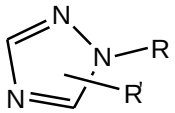
**1, 2, 4-Triazole (3-Substituted):**



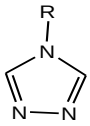
(3) (4) (5)

The preparation of a series of N-heteroarylpiperidine ether-based human NK1 antagonists was described by Ladduwahetty et al. This compounds are orally bioavailable and shown significant developments in potency particularly (3-[{(2S, 3S)- 3-(((3, 5-bis (trifluoromethyl) phenyl)methyl)oxy)-2- phenylpiperidino}methyl]-1,2,4-triazole (4) and5- [{(2S,3S)-3-(((3,5-bis (trifluoromethyl)-phenyl) methyl) oxy) -2-phenylpiperidino} methyl]-3-oxo- 1,2,4-triazolone (5) both in vitro and in vivo, compare to the lead carboxamidomethyl)- piperidine ether (3).[7]

**1, 2, 4-Triazole (4-Substituted):**



(6)

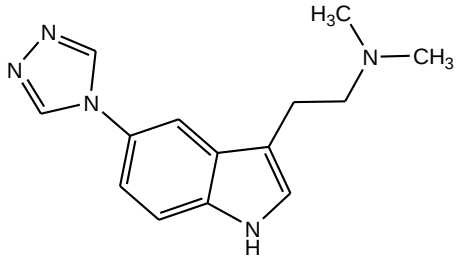


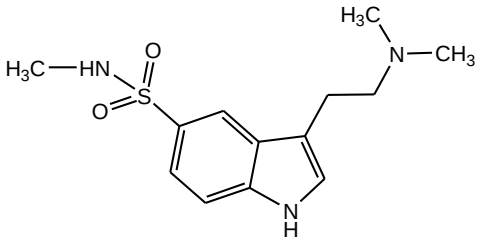
(7)

| | R | R’ |
|---|---|---|
| a. | p-$NO_2C_6H_4$ | H |
| b. | p-$NH_2C_6H_4$ | H |
| c. | p-$CH_3CONHC_6H_4$ | H |
| d. | p-$ClC_6H_4$ | H |

Ainsworth et al have been explored a series of 1- and 4- substituted 1, 2, 4-triazoles[8], for pharmacological screening like convulsant and anticonvulsant activities by the methods as maximal electroshock seizure and subcutaneous pentylenetetrazole seizure tests in rats.The series of compounds (6 a-d) are the p-substituted phenyl compounds among which 1-p-chlorophenyl-1,2,4-triazole is highly active against electroshock seizure but has weak activity against pentylenetetrazole. While compounds o- tolyl (7a) and o-chlorophenyl (7b) were convulsants and o-methoxyphenyl (7c) was an anticonvulsant even at high dose levels.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781



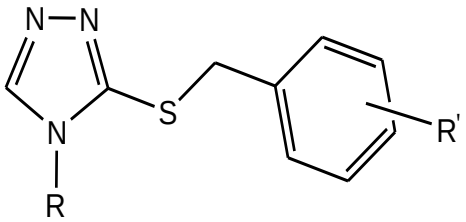




**(**8)(9)

The 1,2,4,triazole derivative (8) is the highly potent, selective and orally active 5-HT1D receptor agonist reported, owing greater potency compared to compound sumatriptan (9) with improved subtype selectivity.

A series of 5- (heterocyclyl) tryptamineshas been recognizedthe similarly substituted, N-4 linked 1,2,4- triazoles as the best indole C-5 substituent for 5-HT1D receptor affinity and selectivity by Sternfeld et al. [9]

**1, 2, 4-Triazole (5-Substituted):**




(10)

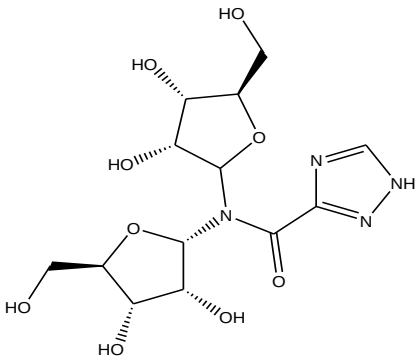
| | R’ |
|---|---|
| a. | H |
| b. | 4-Cl |
| c. | 4-Br |
| d. | 3-Br |
| e | 2-$NO_2$ |
| f | 2,4-$(NO_2)_2$ |
| g | 3,5-$(NO_2)_2$ |

3-(2, 4-dinitrobenzylsulfanyl)-1, 2, 4- triazole (10f) and 3-(3, 5-dinitrobenzylsulfanyl)-1, 2, 4-triazole (10g) are the most active compounds. [1]

**1, 2, 4-triazole (1, 3-disubstituted):**

1-s-Diribofuranosyl- 1, 2, 4-triazole-3-carboxamide (11) against variety of both RNA and DNA viruses in tissue culture. The compounds identifiedas first synthetic broad-spectrum, non-interferon-inducing, antiviral agent.[10]

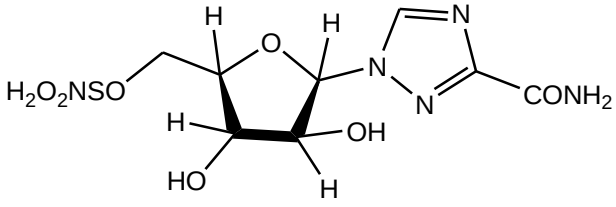
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781



(11)

The triazole nucleoside analogue 1-(5'-O sulfamoyls-D-ribofuranosyl)[1, 2, 4] triazole-3-carboxamide (12), 1-(5'-O-sulfamoyl- s-D-ribofuranosyl) [1, 2, 4] triazole-3-thiocarboxamide, 1-(5'-O-sulfamoyl- s- D-ribofuranosyl) [1, 2, 4] triazole-3-carbonitrile.Many targetcompounds exhibitedimportantin vitro antifungal activities against tested fungi likeAspergillusniger,Candida albicans, Saccharomyces cerevisiae, and Microsporumgypseum.

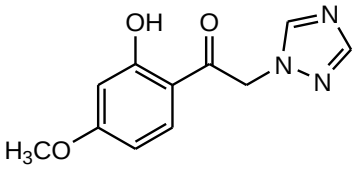
The triazole nucleoside derivatives 1-(5'-O-sulfamoylß- D-ribofuranosyl)[1, 2, 4] triazole-3-carboxamide(16), 1-(5'-O-sulfamoyl- ß-D-ribofuranosyl) [1, 2, 4]triazole-3-thiocarboxamide (17), 1-(5'-O-sulfamoyl- ß-D-ribofuranosyl) [1, 2, 4] triazole-3-carbonitrile (18),were synthesized by Kini et al.[11]



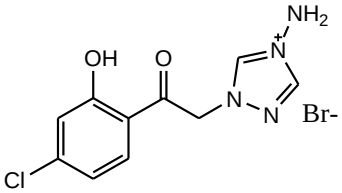
(12)

**1, 2, 4-Triazole (1, 4-Disubstituted):**

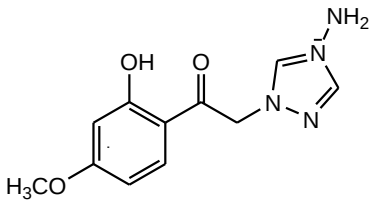
Emami et al have been described 2-Hydroxyphenacyl azole (13) and 2-hydroxyphenacyl azolium compounds (14, 15)as new class of azole antifungals.[12].Among this most target compounds exhibited significant in vitro antifungal activities against fungi like Aspergillusniger, Candida albicans, Saccharomyces cerevisiaeand Microsporumgypseum.



(13)



(14)

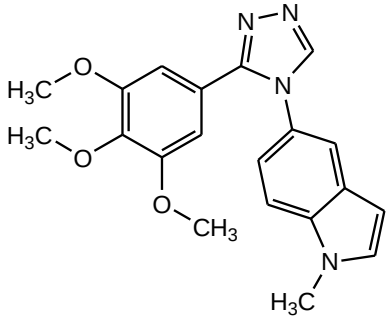


(15)

**1, 2, 4-Triazole (3, 4-Disubstituted):**

Agroup of tubulin polymerization inhibitors that enclose the 1, 2, 4-triazole lead to keep the biologically active structures afforded by the cis double bond in combretastatin A-4 was described by Zhang et al[13]. Many of the compounds shown potent cytotoxicity against a variety of cancer cells including multi-drug-resistant cancer cell lines and tubulin polymerization inhibitory activity.The N-methyl-5-indolyl moiety when attached to the 1, 2, 4-triazole core, as established by compound (16), owingoptimum properties in this series.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

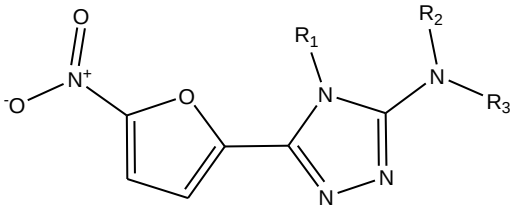


(16)

**1, 2, 4-Triazole (3, 5-disubstituted):**

5-(5-nitro- -furyl)-1, 2, 4-triazole (17)series with their biological activity as potent urinary tract antibacterial agents was synthesized and tested by Akerblomet al[14]. Many of the derivatives showed a higher antibacterial activity than nitrofurantoin especially against gram-vebacteria.

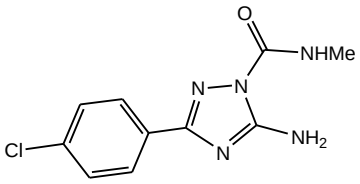
$R_1 = R_2 = R_3 = H$



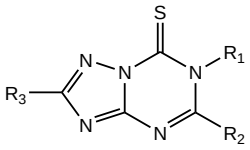
(17)

**1, 2, 4-Triazole (1, 5-Disubstituted):**

Akahoshi et al[15] synthesized series of inhibitors in extension of their preceding work on eosinophilia inhibitors, which comprised of 5-amino-1-[(methylamino) thiocarbonyl]- 1H-1,2,4-triazole derivatives(18) and a newly developed series of 1,2,4-triazolo[1,5-a]-1,3,5-triazine derivatives(19).



(18)



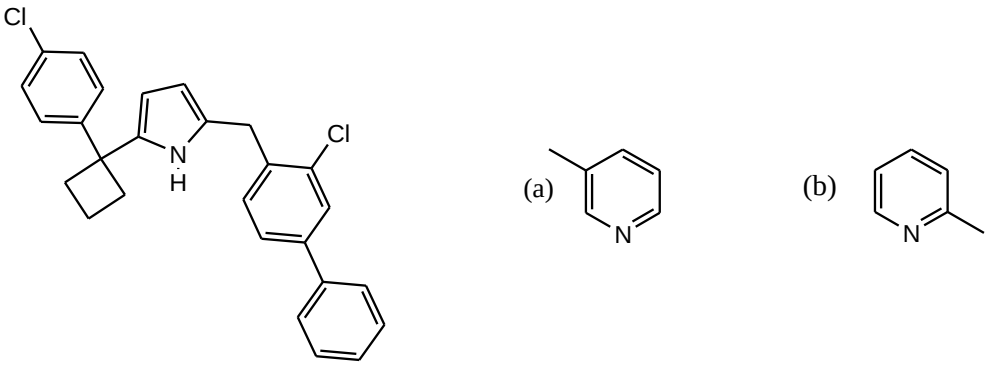
(19)

| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| a | $CH_3$ | H | $C_6H_4$-(4Cl) |

**1, 2, 4-Triazole (4, 5-Disubstituted):**

4-methyl-5-phenyl-(1, 2, 4) triazoles (20)is a selective inhibitors of 11β- hydroxysteroid dehydrogenase type1 (11β-HSD1) was identified Zhu et al[16]. They were active in vitro and in vivo mouse pharmacodynamics model.

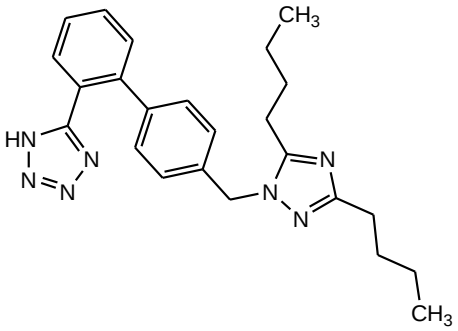
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781




(20)

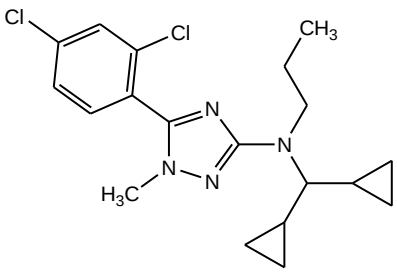
**1, 2, 4-triazole (1, 3, 5-trisubstituted):**

Some novel analogs of lH-1, 2, 4-triazole consisting biphenyl methyl group attached to carbon and the butyl group were attached to the adjacent nitrogen wasdescribed by Reitz et al[17].Also they were potent angiotensin II receptor antagonists. The in vivo properties of dibutyl analog (21) were noted.




(21)

The synthesis of 1-alkyl-3- dialkylamino-5-phenyltriazoles (22) as major products was described by Chen et al [37].




(22)

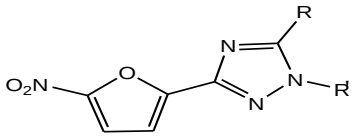
**1, 2, 4-Triazole (2, 3, 5-Trisubstituted):**

Burch et al[18] were reported the synthesis of series 3-alkyl-5-(5-nitro-2-furyl)-l, 2, 4-triazoles (23).Among them many of the analogue owed broad spectrum antibacterial activity in vitro against both gram positive and gram negative bacteria, except Pseudomonas aeruginosa. The Compounds with the above substituents exhibitedmaximum biological activity.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

R=$CH_3$, $C_2H_5$, CH $(CH_3)_2$

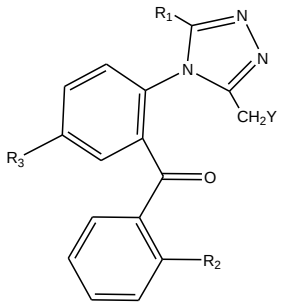
R'=H



(23)

**1, 2, 4-triazole (3, 4, 5-trisubstituted):**

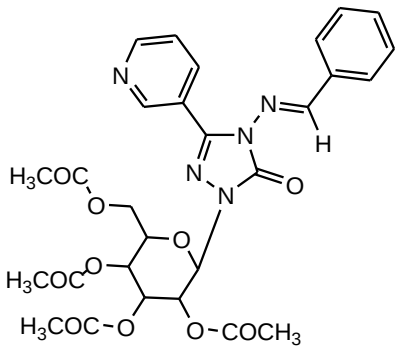
2- [(alkylaminomethyl)-4H-1, 2, 4-triazole-4-yl] benzophenones (24) series were synthesized by Gall et al[19].This analogues were shown potential sedative and muscle relaxing activity, similar as prodrugs of triazolobenzodiazepines.



(24)

**1, 2, 4-Triazole (1, 3, 4, 5-Tetrasubstituted):**

Glucosidation of many 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 reported by Nasser et al[20].It was followedby a chromatographic separation made thecorresponding N- and S-s- D-glucosides.The analogue (25)exhibitedmaximum inhibitory effect against Staphylococcus aureus, Candida albicans, Aspergillusfumigatus, Bacillus subtilis, and Escherichia coli.

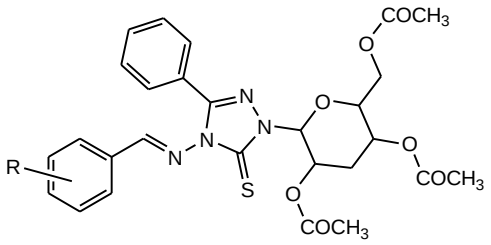


(25)

**1, 2, 4-Triazole (2, 3, 4, 5-tetrasubstituted):**

D-glucopyranosyl- 1, 2, 4-triazole-3-thione derivatives (26a–d) series were synthesized and screened by Li et al[21]. The Schiff bases thereforefoundsuccessively afforded similarcompounds with the substituents as introduced in its past derivatives.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

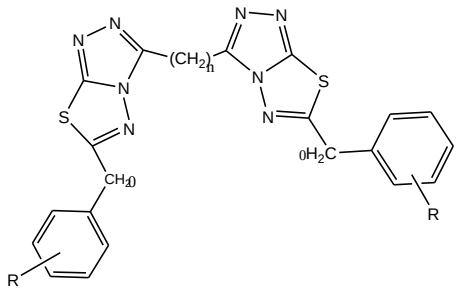


| | R |
|---|---|
| a. | H |
| b. | 4-Cl |
| c. | 3-$OCH_3$ , 4-OH |
| d. | 4-OH |

(26)

**Fused Ring System:**

A several compounds as bis-[4-amino-5-mercapto-1, 2, 4-triazol-3-yl] alkanes (27) was synthesized by Holla et al[22]. Which were converted into bis-[1, 2, 4-triazolo [3, 4-b]- 1,3,4-thiadiazol-4-yl] alkanes.



R=2 Cl n=2

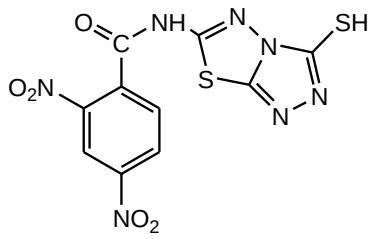
(27)

**III.Applications and Biological Activities**:

1,2,4-Triazole scaffold and its analogue are a potentialkinds of derivativescomprisingindustrial, agricultural, environmental, and pharmacological activities, including anti-inflammatory, antimicrobial, anticonvulsant, antibacterial, antitubercular, anticancer, anti-oxidant, antiviral and antifungal activities.[3]

**Industrial Application:**

It has been reported that specific selective triazole derivatives have been used as light emitting diodes like in electroluminescent devices. Variouskinds of triazole analogues have been used to enhance the efficiency of cooling fluids (lubricant oil), for example 2-mercapto-1, 2, 4-triazole-2,4- dinitrobenzamide(28).[23]



(28)

**Agricultural Applications:**

An extensive series of azole herbicides have been explored that are containing higher level of bioactivity, flexibility, crop tolerance and low levels of toxicity to human being. Many azole analoguesfind application in the plant protection technology as pesticides.[24]

In vitro activity of Etaconazole on fungi which producing summer disease of apple have been evaluated by Sutton et al. [25]While Diniconazole fungicides residues have been detected by Amer et al[26] in tomatoes and green beans by capillary gas chromatography.

**Pharmacological activities:**

Since previous many decades 1, 2, 4-triazoles and its biological properties of have been explored and synthesis and characterization of 1, 2, 4- Triazole

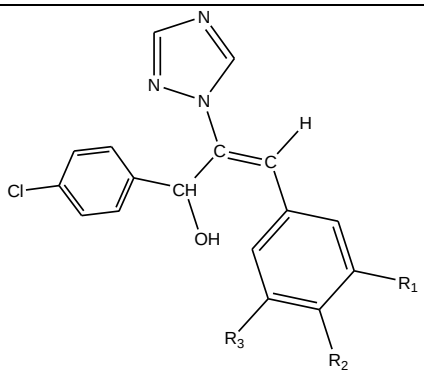
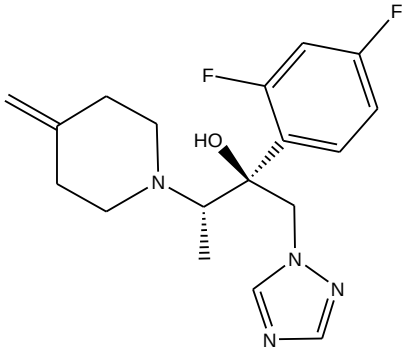
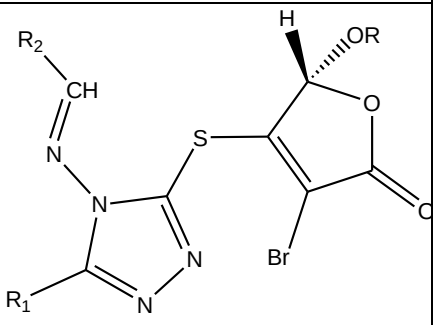
International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

and its derivatives with different biological activities illustrated.

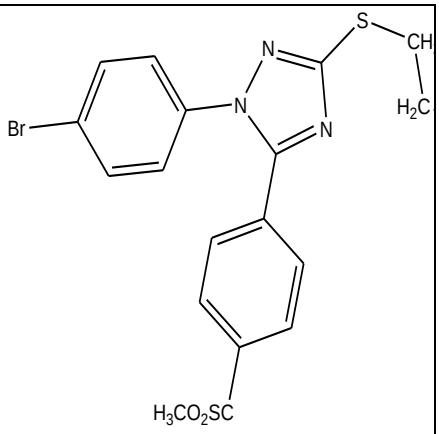
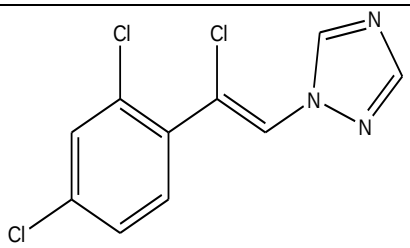
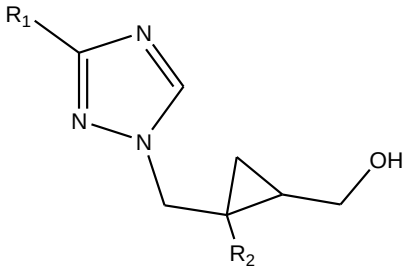
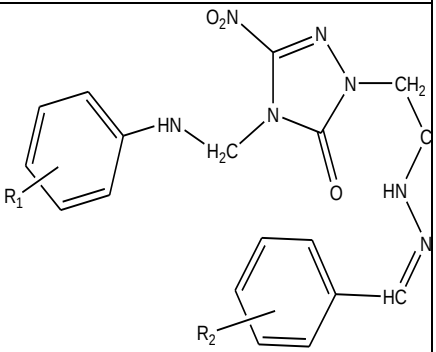

**Figure 1: biological properties of 1, 2, 4-triazoles**

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

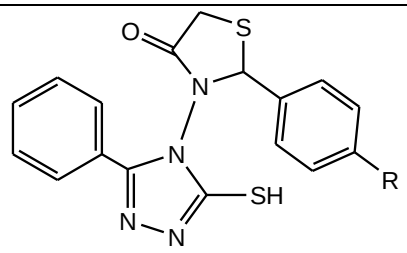
**Table No: 2, Pharmacological activities of 1, 2, 4 Traizoles and its derivatives.**

| Activity | Description | 1, 2, 4- Triazole derivatives | |
|---|---|---|---|
| **1. Antibacterial Activity** | Substituted-(+)α-(4-chlorophenyl)-β-(phenylmethylene)-1H-1,2,4-triazole-1-ethanols) have been synthesized by Uchil et al[27]. It is used as bacteriostatic agent. |  | a:$R_1$=$R_2$=$R_3$=Cl<br>b:$R_1$=Br, $R_2$=$R_3$=H<br>c:$R_1$=$R_2$=$R_3$=O<br>d:$R_1$=$R_3$=H,$R_2$=$SCH_3$<br>e:$R_1$=$OC_6H_5$, $R_2$=$R_3$=H<br>f:$R_1$=$OCH_3$, $R_2$=OH $R_3$=H<br>g:$R_1$=$R_3$=H, $R_2$=OH<br>h: $R_1$=$R_2$=$OCH_2O$,$R_3$=H<br>i:$R_1$=$R_3$=H,$R_2$=$N(CH_3)$ |
| **2.Antifungal Activity** | Tatsumi et al. was studied the mechanism of action of triazole antifungal, with Trichophytonmentagrophytes and Candidaalbicanscompared to Efinaconazole (20) dose-dependently decreased ergosterolproduction and accumulated 4,4-dimethylsterols and 4α-methylsterols.[28] |  | |
| **3.Anticancer and Antitumor Activities** | Anticancer activity of 12 derivatives of 1,2,4-triazole Schiff's bases bearing γ-substituted butenolide Moiety were produced and screened in vitro by Li et al [29] |  | |

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

| | | |
|---|---|---|
| **4.Anti-inflammatory Activity** | A series of diaryl-1,2,4-triazole and N-hydroxyurea (27) were produced and screened for anti-inflammatory agents, and displayed promising analgesic activity were reported by Jiang et al.[30] |  |
| **5.Anticonvulsant Activity** | Wingrove et al. demonstrate the activity of Loreclezole (second-generation antiepileptic drug) is based on the interaction between the triazole moiety and the amide group of asparagine which is located on the β2 subunit of the GABAA receptor.[31] |  |
| **6. Antiviral Activity** | 1,2,4-triazole acyclic cyclopropane nucleoside derivatives were synthesized and screened by K. Benci et al.[32] |  |
| **7.Antitubercular Activity** | For development of novel anti tubercular drugs, importanttarget is tubercule bacillus. MasteMeenaxi et al. were studied the antitubercular activity of 1,2,4-triazole derivatives.[33] |  |

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

| | | |
|---|---|---|
| **8.Antioxidant Activity** | Series of 4-amino-5-phenyl-4H-1,2,4-triazole-3-thiol derivatives have been synthesized and screened for antioxidant activity by A. Abdul Hameed and F. Hassan [34] |  |

## II. CONCLUSION:

Triazoles and its derivatives attributed extreme attention for prominent biological and medicinal significance in field of medicinal chemistry. Human being is affected with so many disorders and there is serious need of medicines to improve the quality of life of individuals. This review explore chemistry and rational structural diversity with pharmacophore as 1, 2, 4 triazole, which signify huge therapeutic application. The heterocycle 1,2,4tiazole is promising lead having remarkable synthetic applicability and biological activities. This will help aresearcher to design suitable structural modification and implement new approaches towards exploring novel drugs with better efficacy.

**Abbreviations:Not Applicable**

**Conflicts of Interest**

The author declared no conflict of interests.

**Acknowledgements:**This review is financially supported by the IQAC ASPIRE funded minor research project grant, SavitribaiPhule Pune University, Pune.

## REFERENCE:

[1]. Banerjee, S., Ganguly, S., Sen, K. K., & India, B. W. B. (2013).A review on 1, 2, 4-triazoles. Journal of Advanced Pharmacy Education & Research Jul-Sept, 3(3).

[2]. Mothes-Wagner, U., Reitze, H. K., & Seitz, K. A. (1990). Environmental actions of agrochemicals 1.Side-effects of the herbicide 3-amino-1, 2, 4-triazole on a laboratory acarine/host-plant interaction (Tetranychusurticae/Phaseolus vulgaris) as revealed by electron microscopy. Experimental & applied acarology, 8(1), 27-40.

[3]. Shneine, J. K., &Alaraji, Y. H. (2016). Chemistry of 1, 2, 4-triazole: a review article. Spectroscopy, 9(9b), 9c.

[4]. Kaur, P., Kaur, R., &Goswami, M. (2018). A review on methods of synthesis of 1, 2, 4-triazole derivatives. IRJP, 9, 1-35.

[5]. Pautus, S. M., Coogan, M. P., & Simons, C. (2007). Synthesis and CYP26A1 inhibitory activity of 1-[benzofuran-2-yl-(4-alkyl/aryl-phenyl)-methyl]-1H-triazoles and amino-benzooxazole derivatives.In Abstracts of Papers-American Chemical Society (Vol. 233, p. 636).American Chemical Society.

[6]. Sun, Q. Y., Zhang, W. N., Xu, J. M., Cao, Y. B., Wu, Q. Y., Zhang, D. Z., ... & Jiang, Y. Y. (2007). Synthesis and evaluation of novel 1-(1H-1, 2, 4-triazol-1-yl)-2-(2, 4-difluorophenyl)-3-[(4-substitutedphenyl)-piperazin-1-yl]-propan-2-ols as antifungal agents.European journal of medicinal chemistry, 42(8), 1151-1157.

[7]. Ladduwahetty, T., Baker, R., Cascieri, M. A., Chambers, M. S., Haworth, K., Keown, L. E., ...& Hargreaves, R. J. (1996). N-Heteroaryl-2-phenyl-3-(benzyloxy) piperidines: a novel class of potent orally active human NK1 antagonists. Journal of medicinal chemistry, 39(15), 2907-2914.

[8]. Ainsworth, C., Easton, N. R., Livezey, M., Morrison, D. E., & Gibson, W. R. (1962). The anticonvulsant activity of 1, 2, 4-triazoles. Journal of Medicinal Chemistry, 5(2), 383-389.

[9]. Sternfeld, F., Baker, R., Broughton, H. B., Guiblin, A. R., Jelley, R. A., Matassa, V. G., ... & Street, L. J. (1996). The chemical evolution of N, N-dimethyl-2-[5-(1, 2, 4-triazol-4-yl)-1H-indol-3-yl] ethylamine (L-741,604) and analogues: Potent and selective agonists for 5-HT1D receptors. Bioorganic & medicinal chemistry letters, 6(15), 1825-1830.

[10]. Witkowski J.T., Robins R.K., Sidwell R.W., Simon L.N. Design, Synthesis, and Broad Spectrum Antiviral Activity of 1-β-D-Ribofuranosyl-1,2,4-triazole-3- carboxamide

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 414-430 www.ijprajournal.com ISSN: 2249-7781

and Related Nucleosides. J. Med. Chem.1972; 15(11):1150-1154.

[11]. Kini G.D., Henry E.M., Robins R.K., Larson S.B., Man J.J., Berens R.L., Bacchi C.J., Nathan H.C., Keithly J.S. Synthesis, structure, and antiparasitic activity of sulfamoyl derivatives of ribavirin. J. Med. Chem.1990; 33:44-48.

[12]. Emami S., Foroumadi A., Falahati M., Lotfali E.,Rajabalian S., Ebrahimi S., Farahyar S., Shafiee A. 2- Hydroxyphenacyl azoles and related azolium derivatives as antifungal agents. Bioorg. Med. Chem. Lett.2008; 18:141–146.

[13]. Zhang Q., Peng Y., Xin I.W., Keenan S.M., Arora S., Welsh W. J. Highly Potent Inhibitors of Methionine Aminopeptidase-2 Based on a 1,2,4-Triazole Pharmacophore. J. Med. Chem.2007; 50:749-754.

[14]. Akerblom E.B., Campbell D.E.S. Nitrofuryltriazole Derivatives as Potential Urinary Tract Antibacterial Agents. J. Med. Chem. 1973; 16(4):312-319.

[15]. Akahoshi F., Takeda S., Okada T., Kajii M., Nishimura H., Sugiura M., Inoue Y., Fukaya C., Naito Y., Imagawa T., Nakamura N. Synthesis and Pharmacological Activity of Triazolo[1,5-a]triazine Derivatives Inhibiting Eosinophilia. J. Med. Chem. 1998; 41:2985-2993.

[16]. Zhu Y., Olson S.H., Vosatka A.H., Wright S., Balkovec J.M.4-Methyl-5-phenyl triazoles as selective inhibitors of 11β-hydroxysteroid dehydrogenase type I. Bioorg. Med. Chem. Lett. 2008; 18:3405-3411.

[17]. Reitz D.B., Penick M.A., Norton M.B., Reinhard E.J., Olins G. M., Corpus V.M. lH-1,2,4-triazole Angiotensin II Receptor antagonists:"C-linked" analogs of SC-50560. Bioorg. Med. Chem. Lett.1994; 4(I):105–110.

[18]. Burch H.A. 3-Alkyl-5-(5-nitro-2-furyl)-1,2,4-triazoles and Intermediates. NitrofurylHeterocycles III.1966; 9:405-408.

[19]. Gall M., Hester J.B., Rudzik A.D. Lahti, R. A. 67.Gall, M.; Hester J. B.; Rudzik, A. D.; Lahti R.A. Synthesis and pharmacology of novel anxiolytic agents derived from 2-(dialkylamino)methyl-4H-triazol-4-mercapto-1,2,4-triazol-3-yl] alkanes. IL. Farmaco.1998; 53:574-578.

[20]. Nasser S., Khalil A.M. Efficient synthesis, structure, and antimicrobial activity of some novel N- and S-β-Dglucosides of 5-pyridin-3-yl-1,2,4-triazoles. Carbohydrate. Res.2006; 341:2187–2199.

[21]. Li Z., Gu Z., Yin K., Zhang R., Deng Q., Xiang J. Synthesis of substituted-phenyl-1,2,4-triazol-3-thione analogues with modified D-glucopyranosyl residues and their antiproliferative activities. Eur. J. Med. Chem.2009; 44:4716–4720.

[22]. Holla B. S., Gonsalvesa R., Shenoy S. Studies on some Nbridgedheterocycles derived from bis-[4-amino-5- mercapto-1,2,4 triazol-3-yl] alkanes. IL. Farmaco.1998; 53:574-578

[23]. FA. Hassan,& KW. Younus, "Biological Evaluation of Some Azole Derivatives in Cooling Fluids (Lubricant Oils)," Res. J. Bio.Sci., 7 (1), 48-51, 2012.

[24]. S. Jess, S. Kildea, A. Moody, G. Rennick, AK. Murchie,& LR. Cooke, "European Union Policy on Pesticides: Implications for Agriculture in Ireland, " Pest. Mang.Sci., 70 (11), 1646-1654, 2014.

[25]. G. Guimon, G. Pfister-Guillouzo, A. Bernardini, & P. Viallefont, "A Photoelectron Study (Hel, Hell) of the Tautomeric Equilibrium Chloro- and Bromo-1,2,4- triazole, " Tetrahedron, 36 (8), 1071-1078, 1980.

[26]. IV. Ledeţi, AA. Alexa,& VN. Bercean, "Structural NMR Analysis of Triazolic Compounds Derived from Isonicotinic Acid, " Annals West Uni. Timisoara: Ser. Chem., 20 (1), 81-86, 2011.

[27]. VR. Uchil, & V. Joshi, "Selective Reduction of Substituted α-(1,2,4-Triazol-1-yl)chalcones NaBH4 and Al-Isopropoxide: Synthesis of Substituted (+)α-(4-Chlorophenyl)-β-(phenylmethylene)-1H-1,2,4-triazole- 1-ethanols Having Potential Bacteriostatic and Agro- Based Fungicidal Activity, " Indian J. Chem., 41B, 631-634, 2002.

[28]. Y. Tatsumi, M. Nagashima, T. Shibanashi, A. Iwata, Y. Kangawa, F. Inui, WJJ. Sin, R. Pilla, & Y. Nishiyama, "Mechanism of Action of Efinaconazole, A Novel Triazole Antifungal Agent," Antimicrob.Agent Chemother, 57 (5), 2405-2409, 2013.

[29]. X. Li, XQ. Li, HM. Liu, XZ. Zhou,& ZH. Shao, "Synthesis and Evaluation of Antitumor Activities of Novel Chiral 1,2,4-Triazole Schiff Bases Bearing γ- Butenolide

Moiety, ” Org. Med. Chem. Lett., 2 (26), 1-5, 2012

[30]. 30. B. Jiang, X. Huang, H. Yao, J. Jiang, X. Wu, S. Jiang, Q. Wang, T. Lu, & J. Xu, “Diaryl-1,2,4-Triazoles bearing N-Hydroxyurea Moiety as Dual Inhibitors of Cyclooxygenase-2 and 5-Lipoxygenase, ” Org. Biomol. Chem., 12 (13), 2114-2127, 2014.

[31]. 31. PB. Wingrove, KA. Wafford, C. Bain, & PJ. Whiting, “The Modulatory Action of Loreclezole at the γ-Aminobutyric Acid Type A Receptor is Determined by a Single Amino Acid in the β2 Subunit,” Proc. Nat. Sci., USA, 91, 4569-4573, 1999.

[32]. 32. K. Benci, T. Suhina, L. Mandić, SK. Pavelić, Paravić AT., K. Pavelić, J. Balzarini, K. Wittine, & M. Mintas, “Novel 1,2,4-Triazole and Purine Acyclic Cyclopropane Nucleoside Analogues: Synthesis, Antiviral and Cytostatic Activity Evaluation, ” Antiviral Chem. Chemother., 21, 221-230, 2011.

[33]. 33. MM. Meenaxi, R. Ainapure, PB. Patil, & AR. Bhat, “Triazolone and Their Derivatives for Anti-Tubercular Activities,” Asian J. Res. Chem., 4 (7), 1050-1054.2011

[34]. 34. A. Abdul Hameed, & F. Hassan, Synthesis, Characterization and Antioxidant Activity of Some 4-Amino-5-phenyl-4H-1,2,4-triazole-3-thiol Derivatives,” Int. J. App. Sci. Tech., 4 (2), 202-211. 2014