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Tetrazole as a Core unit Biological evaluation Agent

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A B S T R A C T

The article is aimed to discuss characterize and screening the biological activity of a series of Tetrazole as a Core Biological evaluation Agent Tetrazole are of great biological interest, especially as anti-tubercular antibacterial. The important and structural diversity of biologically active antibiotics led to the development of many novel methods for the construction of appropriately substituted Tetrazole with attendant control of functional group and stereochemistry. Tetrazole derivatives are reported to show a variety of antimicrobial, anticonvulsant, anti-inflammatory and cardiovascular activities, antimycobacterial activity, antibacterial activity, antihypertensive activity.

Keywords: Antibacterial activity, Antifungal activity, Schiff bases.

A R T I C L E I N F O

CONTENTS

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1. Introduction

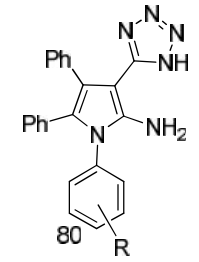
Tetrazoles are class of synthetic organic heterocyclic compounds consisting of five-member ring of four nitrogen and one carbon atom (plus hydrogen). The simplest is tetrazole itself CN4H2.It is white to pale yellow crystalline solid with weak characteristic odour, soluble in water and alcohol. It is acidic in nature due to presence of four nitrogen atoms. Numbering of tetrazoles is as shown below [1-2].Usually tetrazole are explosives. Nature of tetrazoles was unknown. It is used as gas generating agent for air bags. Several tetrazoles are used as pharmaceutical agents.

They undergo electrophilic as well as nucleophilic substitution reactions. Tetrazoles can act as pharmacophore for the carboxylate group, increasing their utility. Angiotensin II blocker often contain tetrazoles, as Losartan and candesartan. A well-known tetrazole is MTT, which is dimethyl thiazolyl diphenyl tetrazolium salt. This tetrazole is used in MTT assay to quantify the respiratory activity of live cells in cell culture, although it kills cells in the process [3-4]. Tetrazoles and its derivatives are used for biological activities such as anti-inflammatory, antibacterial, antifungal, antitubercolous, antiviral, antinociceptive, hypoglycaemic, cyclo-oxygenase inhibitors, and anticancer activities. Tetrazoles are used as catalysts in the synthesis of phosphonates.

Adnan A. B. *et al* has been reported Tetrazolo [1,5-a] quinoline as a potential promising new scaffold for the synthesis of novel anti-inflammatory and antibacterial agents. The four compounds were proved to be active anti-inflammatory agents against indomethacin[5] Umarani Natrajan *et al* reported a facile design and efficient synthesis of schiff's bases of tetrazolo[1,5-*a*] quinoxalines as potential anti-inflammatory and anti-microbial agents and few of them exhibited promising activity[6].Md

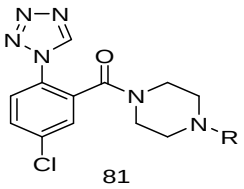
Hari N. Patil *et al* has reported synthesised a series of 1-substituted tetrazole derivatives (81-83). Synthesised compounds were screened for their antibacterial and

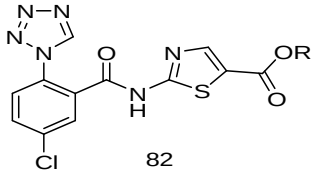
Salahuddin *et al* reported the synthesis of some novel benzo thieno[2, 3-d] pyrimidines and synthesized compounds are screened for biological evaluation and are active against the bacteria like *Bacillus subtilis, Bacillus pumilis, Escherichia coli and Staphylococcus aureus* but the Thieno[2,3-d] pyrimidines derivative containing tetrazole ring shows moderate antibacterial activity[7]. Mosaad Sayed Mohamed *et al* reported the synthesis of *N*-(3-cyano-1-(3-methylphenyl)-4,5-diphenyl-1*H*-pyrrol-2-yl)-acetamides (**80**), 2-amino-1-(4-methoxyphenyl)-4,5-diphenyl-3-tetrazolo-1*H*pyrroles (**80**) and found to possess potent antimicrobial activity[8].



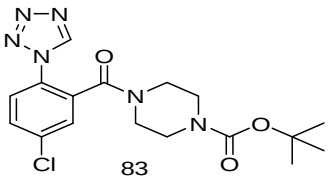
R= H, 2-CH_3, 3-CH_3, 4-OCH_3

antifungal activity**.** In this study, thiazole attached tetrazole derivatives were most active than the piperazine attached tetrazole derivatives [9].

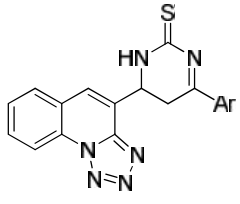




R=H, CH_2CH_3



Adnan A. Bekhit *et al* has reported Three series of tetrazolo[1,5-a]quinoline derivatives (84) have been synthesized. The newly synthesized compounds were evaluated for their anti-inflammatory and antimicrobial activities. Four compounds were proved to be as active as indomethacin in animal models of inflammation [10].



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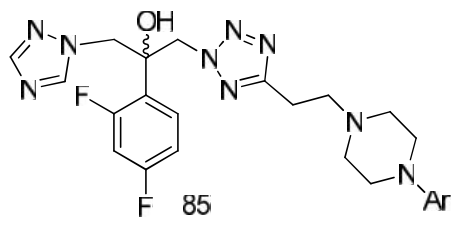
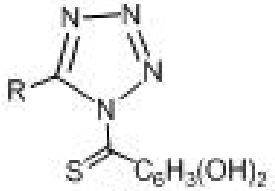


85

Upadhyaya R.S. *et al* reported synthesis and antifungal activity of novel substituted tetrazoles. The derivatives containing piperidine are found to be highly active [11].

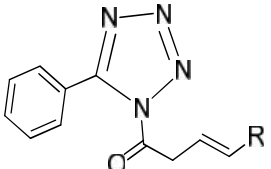
Joanna Matysiak *et al* reported Various 1-(2,4-dihydroxy thiobenzoyl)imidazoles, -imidazolines and –tetrazoles (86) were synthesized and tested for their in vitro antifungal activity. Compounds were prepared by the reaction of sulfinyl-bis-(2,4-dihydroxythiobenzoyl) with properly substituted azoles.

The MIC values against the Candida albicans ATCC 10231 strain, the azole-resistant clinical isolates of C. Albicans and non- Candida species were determined. Tetrazole derivatives were the most active against C. albicans , imidazoline derivatives against non-Candida species. All compounds showed higher activity than that of comparable drugs [12].



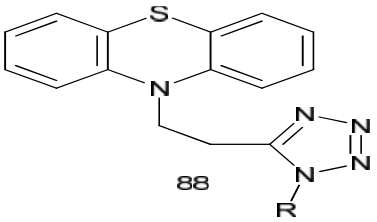
86

Mohite Popat B. et *al* has reported Synthesis and antifungal activity of 3-aryl-1-(5-phenyl-1*H*-tetrazol-1-yl)prop-2-en-1-one (87) and evaluated for antifungal activity using cup and plate method in which compound containing chloro group are highly active[13].



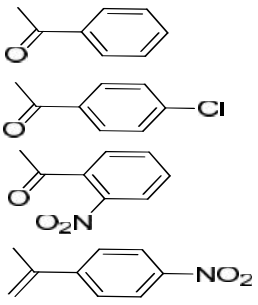
87

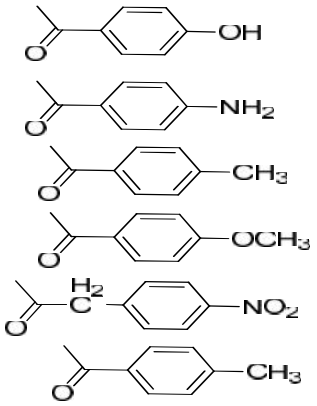
Rajasekaran A. *et al* [14] has reported on synthesis and analgesic evaluation of some 5-[b-(10-phenothiazinyl)ethyl]-1-(acyl)-1,2,3,4-tetrazoles (88).



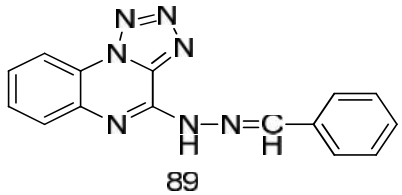
88

R = $O=C-CH_3$, $O=C-CH_2-CH_3$





Umarani Natarajan *et al* reported, A novel synthetic methodology of schiff's bases incorporating tetrazolo quinoxalines .All the newly synthesized heterocycles have been screened for their *in vitro* antimicrobial and anti-inflammatory activities. Few of them exhibited promising activity. The ambient conditions, excellent product yields and easy work up procedures make this synthetic strategy a better protocol for the synthesis of newer Schiff's derivatives [15].



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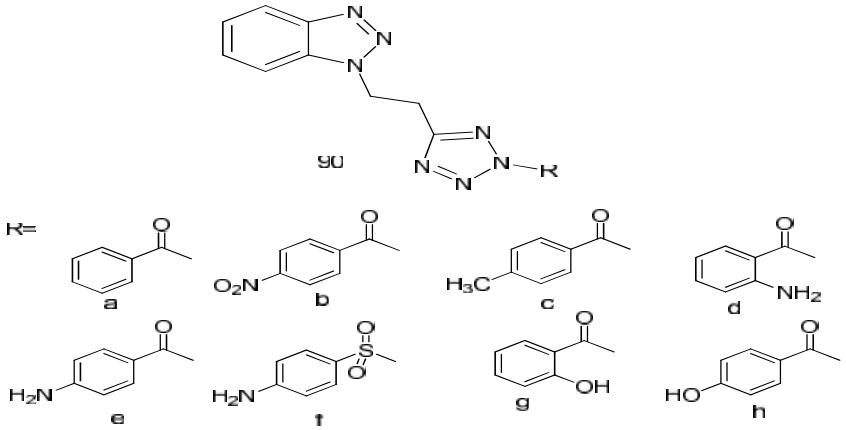
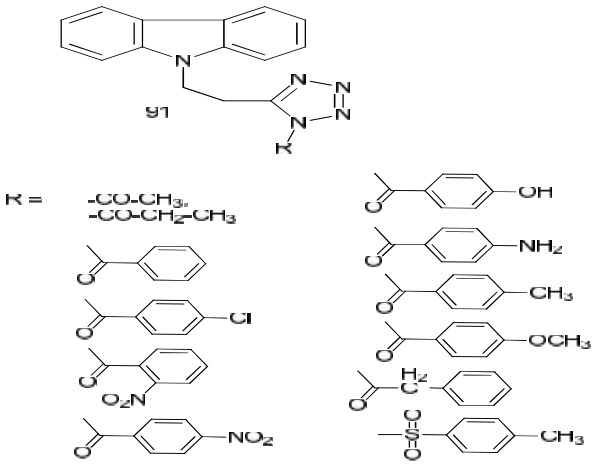
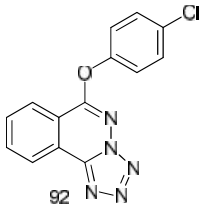
Aiyalu Rajasekaran *et al* reported the synthesis of novel triazole containing tetrazole as anti-nociceptive and anti inflammatory agents in which 5-(2-(1*H*-benzo[*d*] [1,2,3] triazo1-yl) ethyl)-1*H*-tetrazol-1-yl) (4-amino phenyl) methanone (90d) and 5-(2-1*H*benzo[*d*] [1,2,3]triazo-1-yl)ethyl)--1*H*tetrazol-1-yl)(2-hydroxyphenyl)methanone (90g) exhibited significant anti-nociceptive activity. 1-(2-(1-Tosyl--1*H*-tetrazol-5-yl)ethyl)-1*H*benzo[*d*][1,2,3]triazole (90c) and 4,5-(2-(1*H*benzo [*d*][1,2,3] triazo-1-yl)ethyl)-1*H*-tetrazol-1-ylsulfonyl) benzenamine (90f) elicited superior anti-inflammatory activity compared to other synthesized compounds[16].



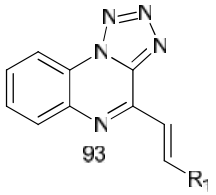
A.Rajasekaran *et al* reported synthesis of Twelve different derivatives of substituted-{5-[2-(1,2,3,4-tetrahydrocarbazol-9-yl) ethyl]tetrazol-1-yl}alkanones (91). The compounds were screened for antinociceptive activity by acetic acid induced writhing method and hot plate method. 1-Phenyl-2-{5-[2-(1,2, 3, 4-tetrahydrocarbazol-9-yl)ethyl]tetrazol-1-yl} ethanone (91k) was found to be the most active compound of the series[17].



Xian-Yu Dun *et al* reported the anticonvulsant activity of 6-(4-chlorophenoxy)-tetrazolo [1,5-a] phtalazine (92) in various experimental seizure models [18].



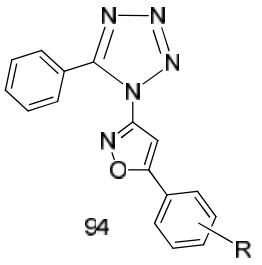
Wagle S. et al reported the synthesis of some new 4-styryltetrazolo[1,5-a] quinoxaline derivatives (93) as potent anticonvulsants[19].



R_1=Phenyl, substituted phenyl

Bhaskar V.H. *et al* have been reported the synthesis, characterization and evaluation of anticancer activity of some tetrazole derivatives in which different tetrazole derivatives containing isoxazole has been synthesized. Among the synthesized tetrazole derivatives, eight compounds have been chosen and screened for their anticancer activity at the National Cancer Institute for testing against a panel of approximately 60 different human tumor cell lines derived from nine neoplastic cancer types. Relations between structure and activity are discussed, the

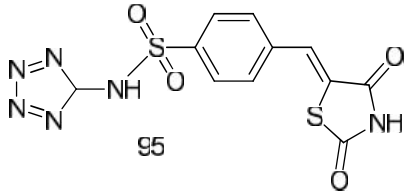
most efficient anticancer compound (4b) was found to be active with selective influence on ovarian cancer cell lines, especially on SK-OV-3 with a growth % of 34.94 [20].



94

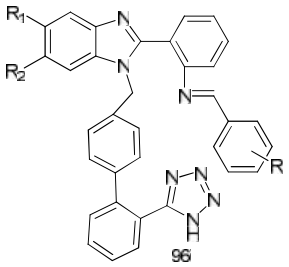
R=H, 2-Cl, 4-Cl, 4-Br, 4-OCH_3, 3-NO_3, 4-CH_3, 4-$N(CH_3)_2$

Pattan S.R. *et al* has synthesized novel 2,4-thiazolidinedione derivatives (95) containing tetrazole ring for their antidiabetic activity. Most of the compounds showed good antidiabetic activity when compared with glibenclamide [21].



95

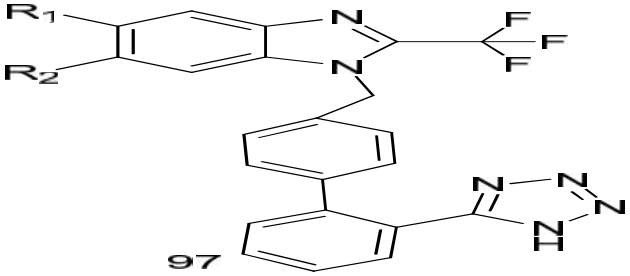
Sharma M.C. *et al* reported the synthesis and pharmacological investigation of some benzylidene-(2-{5,6-substituted-1-[2-(1H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-1H-benzoimidazol-2-yl}-phenyl-amine (96) in the presences of $BF_3 \cdot OEt_2$ catalysts as antihypertensive agents [22,23].



96

1. R=Cl, R_1=Cl, R_2=H
2. R=Cl, R_1=F, R_2=H
3. R=NO_2, R_1=Br, R_2=H
4. R=NO_2, R_1=Cl, R_2=I
5. R=Cl, R_1=I, R_2=CH_3

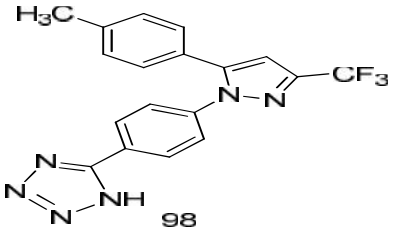
Smita Sharma *et al* reported a Series heterocyclic benzimidazole derivatives bearing of novel 5, 6-Substitute-1-[2'-(1H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-2-trifluoromethyl-1H-benzoimidazol (97) were designed and synthesized for their potential antihypertensive activity [24].



97

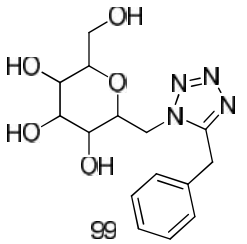
1. R_1=Cl, R_2=COOH
2. R_1=F, R_2=H
3. R_1=Br, R_2=Me
4. R_1=COOH, R_2=F
5. R_1=Me, R_2=F
5. R_1=Cl, R_2=Me

Navidpoor L. *et al* has reported Design and synthesis of new water-soluble tetrazolide derivatives of celecoxib and rofecoxib as selective cyclooxygenase-2 (COX-2) inhibitors [25].



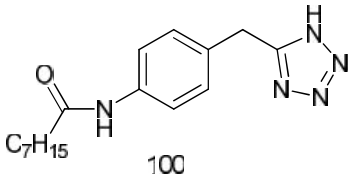
98

Gao Y.L. *et al* has reported design, synthesis and in vivo hypoglycemic activity of tetrazole bearing N-glycosides as SGLT2 inhibitors [26].

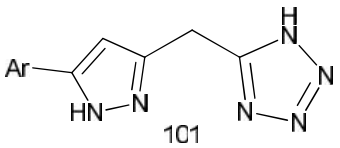


99

Ashoke Sharon *et al* synthesized a series of 5-[(5-aryl-1H-pyrazol-3-yl)methyl]-1H-tetrazoles (100-101)have been synthesized and evaluated for their in vivo antihyperglycemic activity. Some of the synthesized compounds have shown significant glucose lowering activity in male Sprague-Dawley rats in sucrose loaded model. These compounds were also evaluated for their peroxisome proliferator activated receptor agonistic property, but none of them displayed any significant activity [27].

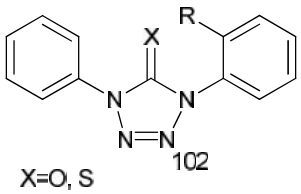


100



101

Synthesis and antiproliferative evaluation of 5-oxo and 5-thio derivatives of 1,4-diaryltetrazoles (102) have been reported by Gundugola A.S. et al [28].



102

X=O, S
R=H, OMe, Cl, CF3, Br,OH

2. Conclusion

a. Furthermore the substitution with phenyl group having a chloro group at p-position showed better activities.

b. The Tetrazoles showed better anti-inflammatory and analgesic activities.

3. Acknowledgements

a. My sincere thanks to UGC authorities for providing financial assistance to continue research in better manner

b. I am very thankful to S.K. University authorities for providing such an environment for doing better research very much.

c. It's my pleasure to express my thanks to Department of Chemistry for giving an opportunity to do research.

d. I express my sincere thanks to Prof L.K Ravindranath, who is giving valuable guidance during my research.

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