Review

A REVIEW ON THE ANTIMICROBIAL, ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY OF 1,2,4-TRIAZOLES.

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ABSTRACT:

Several five membered aromatic systems having three heteroatoms at symmetrical positions such as triazoles have been studied extensively owing to their interesting pharmacological activities. This review article covers the most active triazole derivatives that have shown considerable anti-microbial, analgesic and anti-inflammatory activity. This review article can act as an important tool for organic and medicinal chemists to develop newer compounds possessing triazole moiety that could be better agents in terms of efficacy and safety as emphasis has been laid on the structural activity relationship of the most potent compounds.

KEYWORDS: 1,2,4-triazoles, Antimicrobial, Analgesic and Anti-inflammatory activity.

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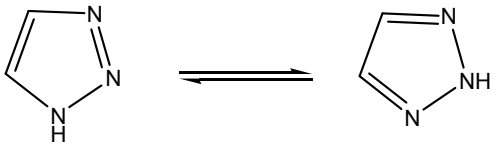
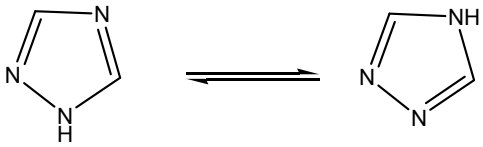
INTRODUCTION:

Nowadays research is concentrated towards the introduction of new and safe therapeutic agents of clinical importance. The heterocycles are enjoying their importance as being the centre of activity. The nitrogen containing heterocycles are found in abundance in most of the medicinal compounds. The success of the imidazole as an important moiety of number of medicinal agents led to the introduction of the triazoles. The triazoles are said to be the isosters of imidazoles in which the carbon atom of imidazole is isosterically replaced by nitrogen. Triazoles are 5 membered rings, which contain two carbon and three nitrogen atoms. According to the position of nitrogen atoms, the triazoles exist in isomeric forms.

Two structural isomeric triazoles are known , the 1,2,3-(1,2,5) and the 1,2,4-(1,3,4), the former being known as osotriazole, and the latter as triazole. Each exists in two disimilar tautomeric forms. The different isomers are characterized by the position of the nascent hydrogen. Thus, 1,2,4-triazoles exist in two isomeric forms i.e. 1H and 4H.



osotraiazoles

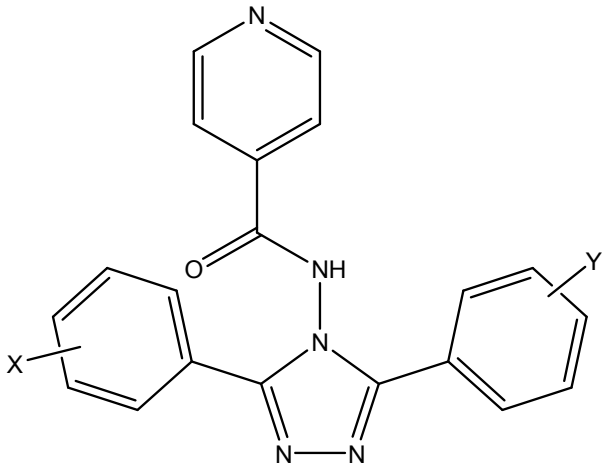


triazoles

1,2,4-Traiazoles shows various biological activities such as antifungal, antibacterial, antitubercular, anticonvulsant, analgesic, anti-inflammatory, antiviral activities. This review article highlights the recent work that has been carried out on 1,2,4-triazoles reporting the antimicrobial, analgesic and anti-inflammatory properties of the triazole moiety.

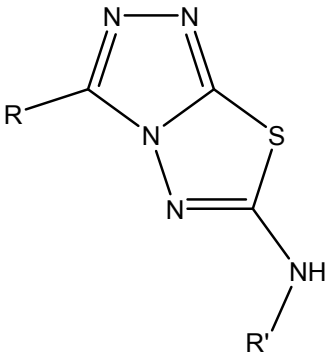
Anti-Microbial Activity.

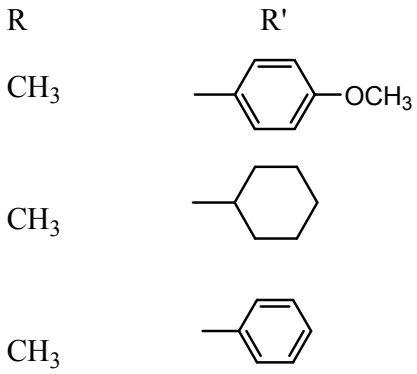
Dhore JW *et al* [1] reported the synthesis of N-((3,5-disubstituted)-4H-1,2,4-triazole-4-ylisonicotinamide by the condenation of substituted 1,3,4-oxadiazole and isoniazid. All the compounds were screened for antibacterial and antifungal activity. Some of them exhibited greater antibacterial activity against E. coli and some exhibited greater antifungal activity for C. albicans.



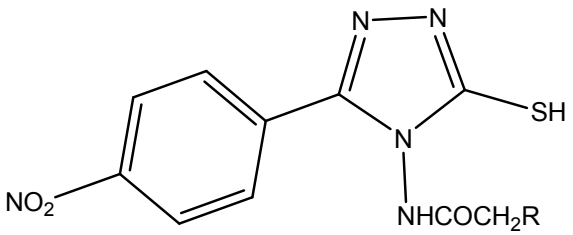
X = $-NO_2$ Y = -OH
X = $-NO_2$ Y = -OMe
X = $-NO_2$ Y = $-NO_2$

Nizamuddin *et al* [2] (1988) synthesized a series of 5-Arylamino-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazolo derivatives by cyclo-dehydrosulphirization of corresponding thiourease. Synthesized compounds were screened for antifungal activity against A. niger and H. oryzae by agar growth technique in which the commercial fungicide Carbendazim was used as standard.





Neeraj *et al* [3] synthesized a series of 4-(substituted ethanoyl)amino-3-mercapto-5-(4-nitrophenyl)-1,2,4-triazole derivatives from 4-nitrobenzoic acid. Newly synthesized compounds were tested for anti-microbial activity. Antibacterial activity was performed by disc diffusion method by using Vancomycin and Amikacin as standard drugs. Similarly prepared compounds were screened for antifungal activity by paper disc method by using Clotrimazole as standard drug.



R = -N(CH_2CH_3)$_2$

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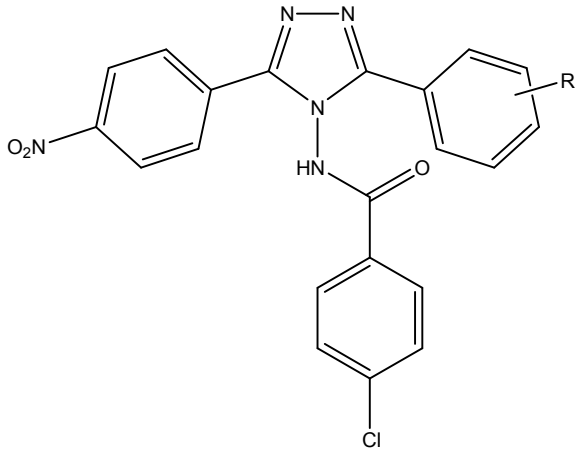
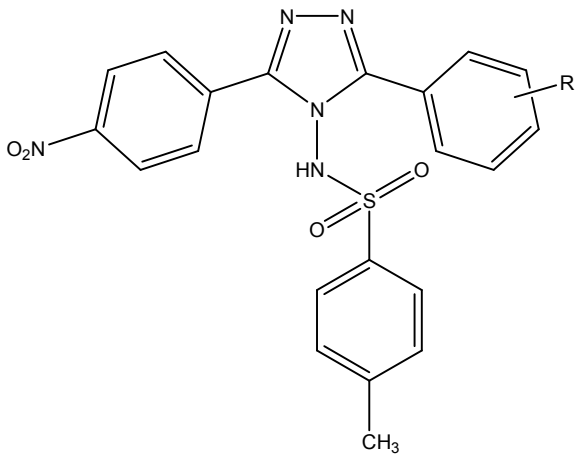
=

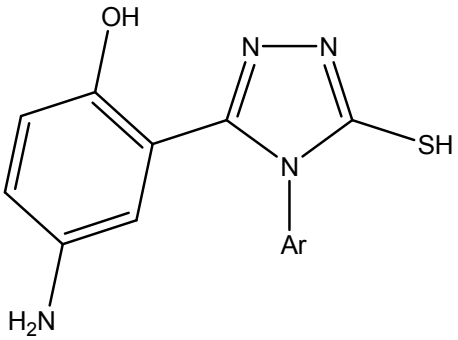
Desai K.R. ***et al*** [4] synthesized different derivatives of 3-((4'-nitrophenyl)-4-(4'-chlorobenzamido)-5-substituted phenyl)-4H-1,2,4-triazole and screened for their antibacterial and antifungal activity. Furacin was used as a standard drug for antibacterial study and Flucazone for antifungal activity.



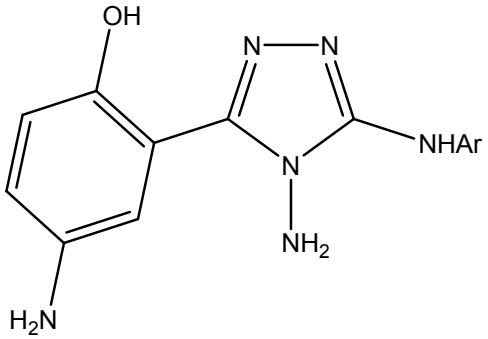


R = o-Cl, o-CH_3, p-Cl, p-OCH_3

Sabir H et al [5] (2008) synthesized various derivatives of 1,2,4-triazole from 5-aminosalicylic acid and evaluated for their antifungal and antibacterial activity. Ofloxacin and Ketocanazole was used as standard drugs for antibacterial and antifungal activity respectievely.



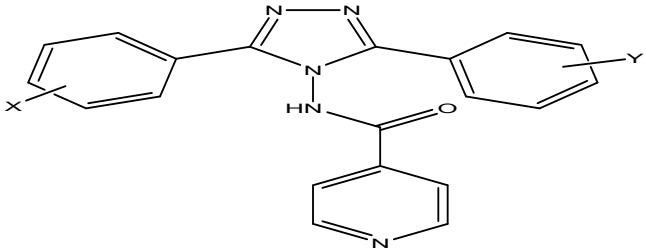
4-amino-2-[4-(4-substituted phenyl)-5-sulphanyl- 4H-1,2,4-triazole-3-yl]phenol



4-amino-2-[4-amino-5-(4-substituted phenyl)amino-4H-1,2,4-triazole-3-yl]phenol

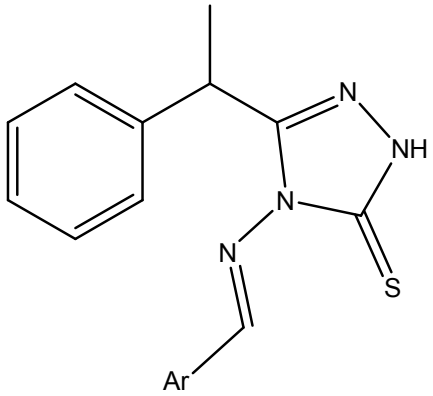
Ar = $C_6H_4CH_3$, C_6H_4F, C_6H_4Br

Shrikanth S.P. et al [6] (2012) prepared some N-(3,5-disubstituted)-4H-(1,2,4-triazole-4-yl)-isonicotinamide by the condensation of substituted 1,2,4-triazole and isoniazid and all the synthesized compounds were tested for antibacterial activity.



X	Y
-H	$-OCH_3$
$-NO_2$	-H
$-NO_2$	-Cl

Kaymakcioglu K et al [7] (2010) synthesized a series of Schiff's bases by reacting 4-amino-5-(1-phenylethyl)-2,4-dehydro-3H-1,2,4-triazole-3-thione and substituted aldehydes and screened them for their antimicrobial activity.



4-[[(4-aryl)methyldine]amino]-5-(1-phenylethyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione

Ar = 4-nitrophenyl, 4-chlorophenyl, 2-hydroxyphenyl

Jubie S et al [8] (2011) synthesized a novel analogue of Ciprofloxacin. Triazole nucleus was synthesized by fusing Ciprofloxacin and Thiocarbohydrazide . Antibacterial activity of synthesized analogue was compared with standard Ciprofloxacin

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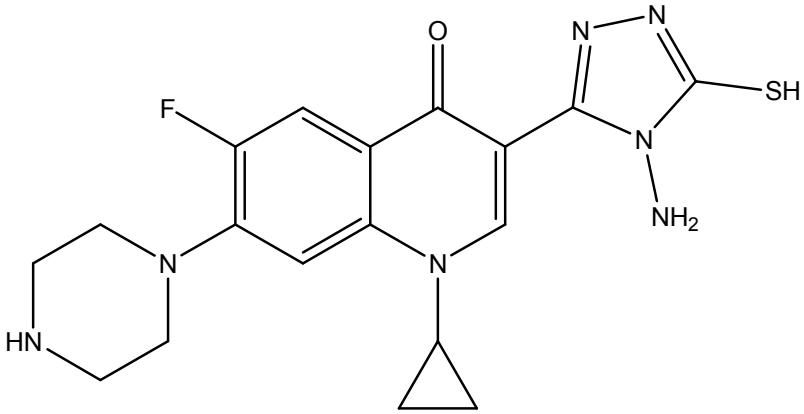
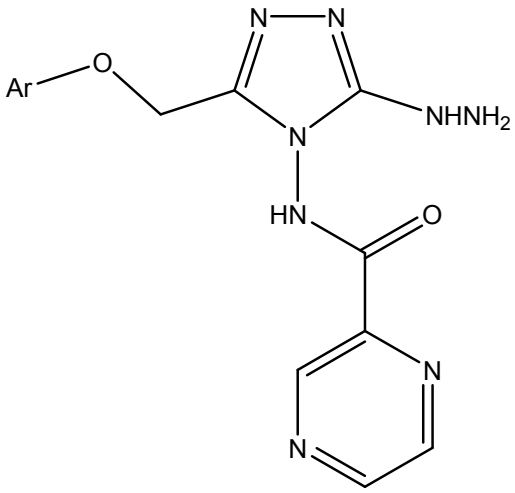


3-[1-cyclopropyl-6-flouro-7-(piperazine-1-yl)quinoline-4(1H)-one]-4-amino-1,2,4-triazole-5-thiol

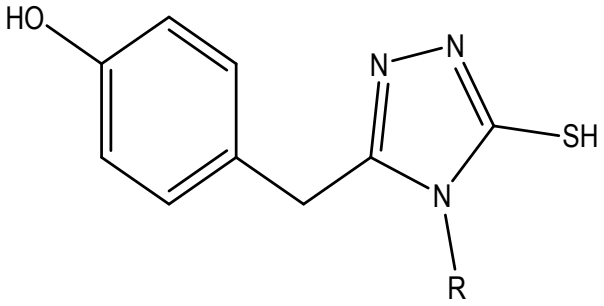
Anti-inflammatory and analgesic activity

Udupi R.H. et al [9] (2007) synthesized 3,4-disubstituted-5-mercapto-1,2,4-triazole from potassium dithiocarbazinate and then these triazoles were converted to their hydrazine derivatives by reacting with hydrazine hydrate. All the synthesized compounds were screened for their antibacterial, antifungal , analgesic and anti-inflammatory activities. Antibacterial activity was performed by cup plate method by using streptomycin and gentamycin as standard drugs. Antifungal activity was performed by poisoned food technique by using Griseofulvin as standard drug. Anti-inflammatory activity was done in albino mice/rats by Hind paw method by using Ibuprofen as standard drug. Analgesic activity was performed in Albino mice by Eddy's Hot plate method by using Ibuprofen as standard.



3-aryloxymethyl-4-(N-pyrazine-2-yl-carboxamido)-5-hydrazino-1,2,4-triazole

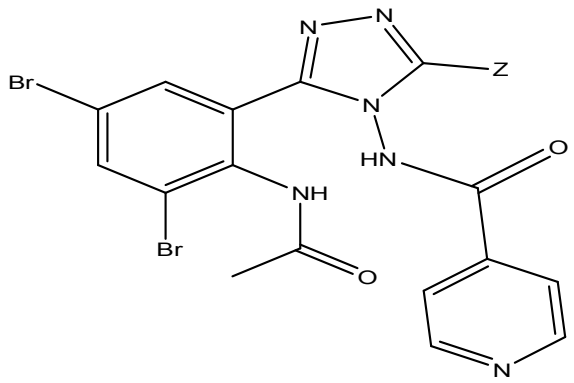
Mohammed A et al [10] (2008) synthesized a series of 1,2,4-triazole derivatives of 4-hydroxyphenyl acetic acid and evaluated for their anti-inflammatory activity by Carragnean induced rat paw edema method by using Ibuprofen as standard drug



5-(4-hydroxyphenyl)methyl-4-aryl/alkyl-3-mercapto-4[H]-1,2,4-triazole.

R = phenyl, 2-chlorophenyl, 4-chlorophenyl

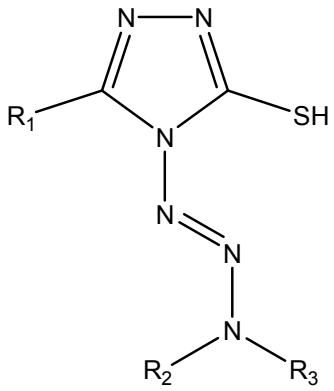
Udupi R.H. et al [11] (2009) synthesized various 1,2,4-triazole derivatives from 2-acetylamino-3,5-dibromo anthranilate by converting into corresponding hydrazide and then to 5-substituted-1,3,4-oxadiazole and finally into 5-substituted-1,2,4-triazole derivatives and all the synthesized compounds were screened for antimicrobial, anti-inflammatory and analgesic activity.



4-(N-pyridyl carboxamido)-3-(3',5'-dibromo-2'-acetylaminophenyl)-5-substituted-1,2,4-triazole.

Z = pyrazinyl, 3-chloropyrazinyl, 2-aminophenyl

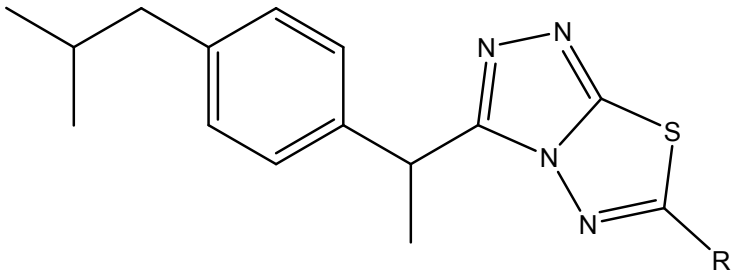
Pradeep K.G. et al [12] (2010) synthesized different derivatives of 3-substituted-4H-1,2,4-triazole by the reaction of 5-alkyl/aryl diazo substituted-4H-1,2,4-triazole-3-thiol with different aliphatic and aromatic amines and screened for anti-inflammatory activity.



3-substituted-4-(3-disubstituted-1-triazenyl)-4H-1,2,4-triazole-5-thiol.

R_1	R_2	R_3
CH_3	H	C_6H_5
CH_3	H	p-$C_6H_4NO_2$
CH_3	H	p-$C_6H_4OCH_3$

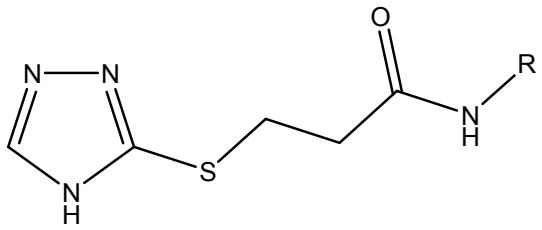
Balakrishna Kalluraya et al [13] (2012) synthesized a series of triazolothiadiazole analogs of Ibuprofen by using microwave energy and screened them for their anti-inflammatory, analgesic and anti-oxidant activity.



3-[1-(4-isobutylphenyl)ethyl]-1,2,4-triazolo-[3,4-b]thiadiazole

R = -CH_3, -C_2H_5, -C_3H_7, 4-BrC_6H_4

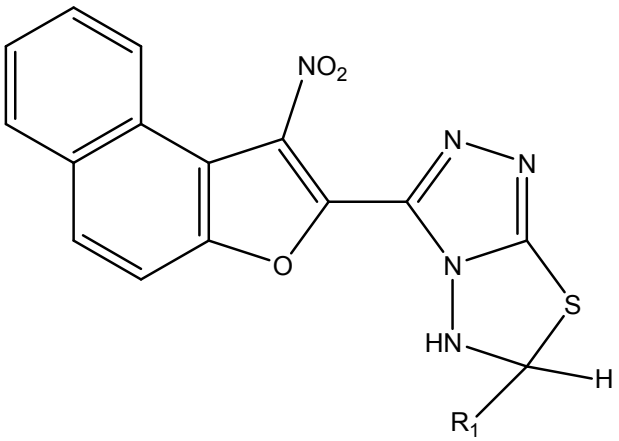
Anil M.M. et al [14] (2010) synthesized various 1,2,4-triazole derivatives from 1-formylthiosemicarbazide. 1,2,4-triazole moiety was prepared from 1-formylthiosemicarbazide and it was condensed with different N-substituted-β-chloropropionamides to obtain different derivatives. The entire synthesized compounds were screened for their analgesic activity.



3-(N-substituted carboxamidoethylthio)-4H-1,2,4-triazole.

R = -C_6H_5, p-ClC_6H_4, p-$NO_2C_6H_4$

Vaidya VP et al [15] (2011) synthesized a series of triazolo thiadiazole derivatives and evaluated them for their analgesic activity by acetic acid induced writhing method by using Swiss albino mice.



3-nitronaphtho-[2,1-b]-furan-2-yl-6-aryl-5,6-dihydro-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazole

R = 4-$OCH_3C_6H_4$, 3-$NO_2C_6H_4$

REFERENCES

1. Dhore. J.W., Pethe. J.B., Wagh. S.P., Thorat. G.D., (2011). Synthesis, Characterization and biological studies of some Triazolyl isonicotinamide. *Scholars Research Library*, 3(1), 407 – 414.
2. Bandana. C., Nirupama T., Nizamuddin., (1988). A convenient and novel synthesis of 1,2,4-triazolo-[3,4,b]-1,3,4-thiadiazoles as potential pesticides. *Agricultural and Biological Chemistry,* 52(5), 1229-1232.
3. Neeraj. U., Sanjay K., Muralidhar. K., Kamal. S., and Pradeep. M., (2011). Synthes and antimicrobial evaluation of some novel 1,2,4-triazole derivatives. Acta Poloniac Pharmaceutica – Drug Research, 68(2), 213-221.
4. Roy. R.U., Desai. A. R., and Desai. K.R., (2005). Synthesis and antimicrobial activity of 1,2,4-triazoles. E-Journal of Chemistry, 2(1), 964 – 972.
5. Sabir. H., Jyoti. S., and Amir. M., (2008). Synthesis and antimicrobial activity of 1,2,4-triazole and 1,3,4-thiadiazole derivatives of 5-amino-2-hydroxybenzoic acid , E-Journal of Chemistry, 5(4), 963 – 968.
6. Shrikanth. S.P., Deepak. M.N., Rameshwar. S.D., and Ganesh. D.T., (2012). Synthesis and Characterization of some N-(3,5-disubstituted)-4H-(1,2,4-triazole-4-yl)-isonicotinamide. IJERA, 2(4), 804 – 807.
7. Kaymakcioglu. B.K., Calisir. M.M., Ozbek. B., and Otuk. G., (2010). Synthesis and antimicrobial activity of some novel Schiff's bases containing 1,2,4-triazole-3-thione. E-Journal of Chemistry, 7(S1), S458 – S464.
8. Jubie. S., Kalirajan. R., and Pavankumar. Y., (2012). Design, Synthesis and Docking studies of a novel Ciprofloxacin analogue as an antimicrobial agent. E-Journal of Chemistry, 9(2), 980 – 987.
9. Udupi. RH., Sudheendra. B., Srinivasalu. N., and Rajesh. V., (2001). Design, Synthesis and biological activity of certain 3,4-disubstituted-5-mercapto-1,2,4-triazoles and their hydrazine derivatives. Bull Korean Chemical Society, 28(12), 2235 – 2240.
10. Mohammed. A., Sadique. A.J., and Harish. Kumar., (2008). Synthesis of some newer analogues of 4-hydroxyphenyl aceticacid as potent anti-inflammatory agents. Journal of the Chinese Chemical Society,55(2), 201 – 208.
11. Pramod. Kumar., Udupi. R.H., and Dubey. P.K., (2009). Synthesis and biological study of substituted 1,3,4-oxadiazole and 1,2,4-triazoles. Internal Journal of Pharm Tech Research, 1(4), 1654 – 1662.

12. Pradeep. K.G., Bhandari. A., Rana. A.C., and Jain. C.B ., (2010). Synthesis of some 3-substituted-4H-1,2,4-triazole derivatives with potent anti-inflammatory activity. Asian Journal of Pharmaceutical and Clinical Research, 3(3), 244 – 246.
13. Sujith. K.V., Balakrishna. Kalluraya., Adithya. A., and Vijaynarayana. K., (2012). Microwave mediated synthesis of triazolothiadiazoles as anti-inflammatory, analgesic and antioxidant agents. Medicinal Chemisrty Research, 21(2), 543 – 551.
14. Anil. M.M., Ravindra. A.F., Rajesh. K.S., and Harish. K.K., (2010). Synthesis and biological screening of novel derivatives of 3-(N-substituted carboxamidoethylthio)-4H-1,2,4-triazoles. Indian Journal of Chemistry, 49B, 1642 – 1647.
15. Shashikala. Devi. K., Ramaiah. M., Vanita. G.K., Veena. K., and Vaidya. V.P., (2011). Synthesis and analgesic activity of triazolothiadiazoles and triazolothiadiazines encompassing 3-nitronaphtho-[2,1-b]-furan. Journal of Chem. Pharm. Res., 3(1), 445 – 451.

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