Advances in Bioresearch
Adv. Biores., Vol 8 (2) March 2017: 22-35
©2017 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.8.2.2235

Advances in Bioresearch

REVIEW ARTICLE

Biological Activities of Thiazide Substituted with Heterocyclic Rings: Review Article

[1]Seyed Vahid Farajolah Hosseini, [2]Samira Arab Salmanabadi
[1]MSc, Department of Chemistry, Shahr-e-Qods Branch, Islamic Azad University, Tehran, Iran
[2]PhD, Faculty Member, Department of Chemistry, Shahr-e-Qods Branch, Islamic Azad University, Tehran, Iran
*Corresponding Author Email: s.arab@qodsiau.ac.ir

ABSTRACT
Appearance and expansion of microbial resistance is one of the serious concerns in public health throughout the world. Thiazoles exhibits broad range of biological activities and was found in many active biological molecules. So far, it has proven that modifications of the thiazole ring are very effective with improved potency and less toxicity so that more than 90 % of novel drugs have the heterocyclic rings. The present study emphasizes the synthesized Thiazoles that have the main biological activities. It can be useful for future design and development of novel pharmaceutical components.
***Key words**: Thiazole derivatives, biological activities*

Received 20/12/2016 Revised 11/01/2017 Accepted 11/02/2017

How to cite this article:
S V Farajolah Hosseini, S Arab Salmanabadi. Biological Activities of Thiazide Substituted with Heterocyclic Rings: Review Article. Adv. Biores., Vol 8 [2] March 2017: 22-35.

INTRODUCTION

Chemical structures have heterocyclic rings that play a main important role in the appearance of active biological activities so that among the 20 million of known chemical components until the end of second millennium AD, more than two-thirds of them are aromatics or have aromatic components. Almost, half of them have heterocyclic structure; more than 90 percent of novel pharmaceutical components have also heterocyclic rings [1].

Heterocyclic systems containing sulfur and nitrogen have been considered due to the physiochemical features in relation with novel drug synthesis [2, 3]. Thiazoles are a heterocyclic component that consists of nitrogen and sulfur atom as a part of five-membered ring of the aromatic. Thiazol and related compounds are called 1, 3- azoles (nitrogen and one of the other heteroatom in a five membered ring). They are isometric with 1, 2 azoles that are called isothiazole in combination with nitrogen and sulfur compounds [4] (figure 1).

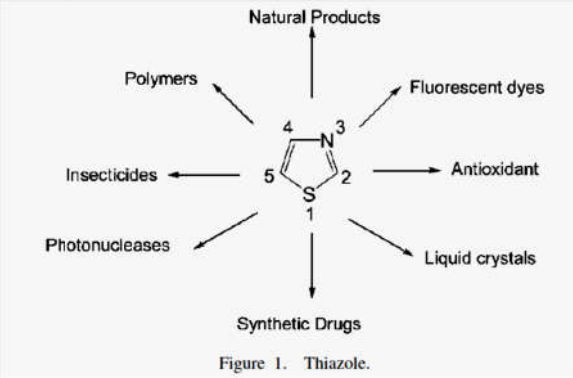


Figure 1. Thiazole.

Figure (1)

Thiazoles are aromatics and based on the delocalization of a lone pair of electron from the sulfur atom that completes required 6 π electrons to satisfy Hucke's rule. Resonance form has been represented in figure 2.

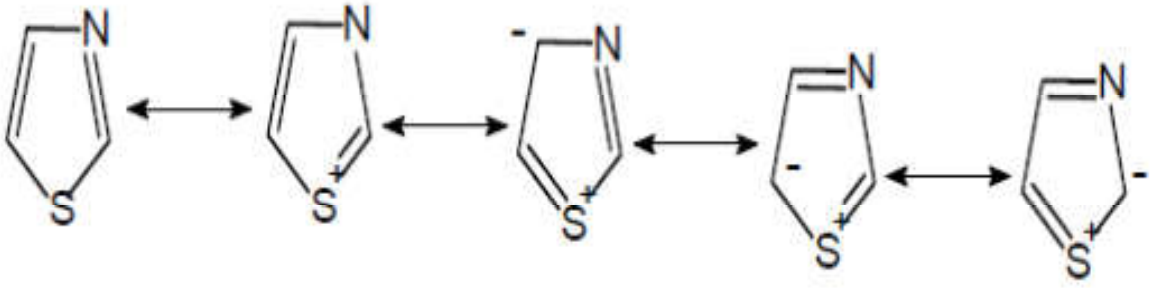


Figure (2)

The molecule due to its different medical properties in many artificial and natural products vastly is used in pharmaceutical activities such as antivirus, anti- cancer, anti-bacterial, anti- fungal, anti-convulsive, anti-tuberculosis, analgesic, anti-Parkinson and anti-inflammatory activity that obviously is seen in existence drugs containing the functional group in market [2,6].

Heterocycles extensively has been used for developing the modern drugs. Therefore, continuous efforts have been done toward designing the artificial methods related to synthesis the heterocyclic compounds [2].

Thiazoles are the main heterocyclic compounds that are found in many potent biologically active molecules such as Sulfathiazol, Ritonavir, Abafungin called as commercial name Abasol, Bleomycine and Tiazofurin. It has been reported that biological activities continuously over the years is in company with Thiazole derivatives (7). In the study, a review on thazols with a large number of biological activities has been represented.

Neuroprotective and antioxidant activities

Koufaki *et al* [8] designed a simulated model that consists of 1, 2- dithiolane derivatives; and t screened them for their neuoprotective activities. Their findings represented that compounds of figure 3 have higher neroprotective properties. Structure- activity relationship showed when Amid replaced with Thiazole ring, the strongest neuropeotectant was represented while 1, 3,4- oxadiazole derivatives had lower power. Therefore, it seems that replacement of amid with six aromatic rings shows the higher neouroprotective activities.

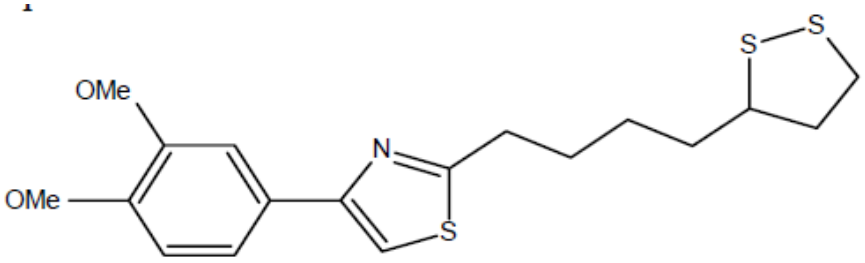


Figure (3)

Shih et al synthesized a serious of sydnonyl substituted with thiazoline and thiazolodionone derivatives and they examined them in view of antioxidant activities. The antioxidant activities of compound 4 derivatives shows the DPPH radical (1, 1- diphenyl- 2 picrylhydrazyl) scavenging activity in comparison with vitamin E.

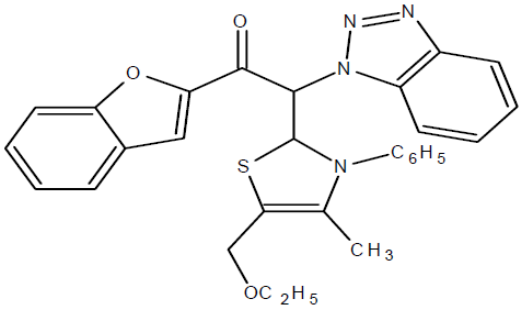


Figure (4)

Antimicrobial activity

Pandeya et al (1999) provided a series of Schiff and Manich bases which is derived from Isatin derivatives and N - [4- (4' chloropheyl) thiazol-2-yl] thiosemicarbazide. Compounds' antimicrobial activities were examined by using agar dilution method against 28 pathogenic bacteria, 8 pathogenic fungi and anti HIV-1 in MT-f. Among the examined compounds, the compound [5] exhibited the most significant antimicrobial activity [10].

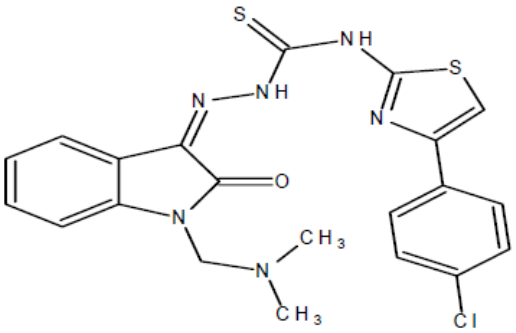


Figure (5)

Shiradkar et al in 2007 have reported a series of N-[4-[(4-amino-5-sulphanyl-4H-1, 2, 4-triazol-3-yl) methyl]-1, 3-thiazol-2-yl]-2 substituted with derivatives of amide. The structures were examined in vitro condition for their primary anti-bacterial activities against *S. aureus, E.coli, P.aeroginosa* and *S.Typhosa* . Thereafter, they were screened for antibercular activity against M. tuberculae H_{37} Rv by using both micro dilution assay principle. Existence components (6, 7) represented the best activities. Shiradkar et al found that the compounds which have demonstrated more than 90 percent of inhibition were obtained by S-alkylation and acetonitrile. In addition, it was stated that the Cyano group may have no role in enhancement of the activity. When the Sulfhydryl group were optimized and examined, it causes to loss the activity (11)

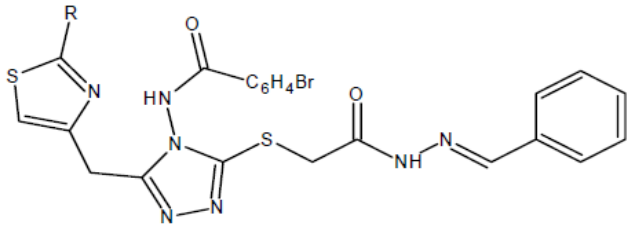


Figure (6) R=$NHCOCH_3$, Ar=3-$NO_2.C_6H_4$[6]

Figure (7) R=$NHCOC_6H_5$, Ar=3-$NO_2.C_6H_4$[7]

Vicini et al (2006) introduced a novel series of 2-thiazolylimino-5-arylidene-4- thiazolidones and evaluated them in vitro condition for their antimicrobial activity against Gram negative and Gram positive, mould and yeast. The results of experiment showed that all compounds especially compound 8 have higher efficiency against Gram positive bacteria. They examined the structure- activity relationship and found that 5- arylidene derivatives exhibited high anti-bacterial effects in comparison with primary compounds so that substituted and substituted 5- arylidene ply the main role in increasing the anti-microbial features in this set of compounds (12).

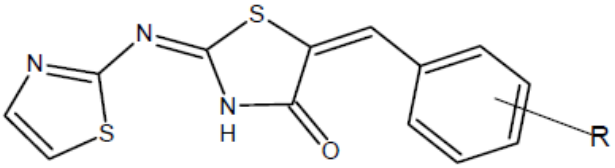


Figure (8): R=H, OH, OCH_3, NO_2, Cl[8]

Abdel- Wahab et al (2009) synthesized the various pyrazolne with thiazole derivatives. Then, they screened them for their antimicrobial and anti-fungal activities against Escherichia Coli and Aspergillusniger. A series of arylidene-2-(4-(4-methoxy/bromophenyl) thiazol-2-yl) hydrazines and 1-(4-(4-methoxybromo phenyl)-thiazol-2-yl)-2 cyclohexylidene/cyclopentylidenehydrazines

Were synthesized by Bharti and they were screened for their antifungal and anti-microbial activities. They found the compounds (9a -c), (10a –c) and (11a- c) are stronger (13).

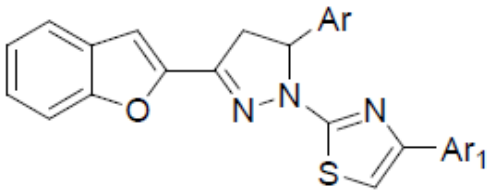


Figure (9)

9a-d[

9a, Ar=Ar_1=Ph

9b, Ar=Ph, Ar_1=4-Br.C_6H_4

9C, Ar=4-Cl.C_6H4, Ar_1=Ph

9d, Ar=4-Cl.C_6H_4, Ar_1=4-Br.C_6H_4

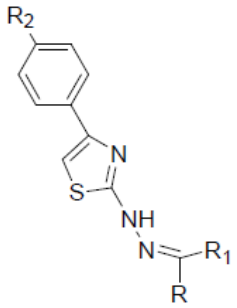


Figure (10)

10a-c[

10a, R=H, R_1=C_6H_5, R_2=OCH_3

10b, R=H, R_1=C6H_5, R_2=Br

10c, R=C_6H_5, R_1= - CH (OH) C6H5, R_2=Br

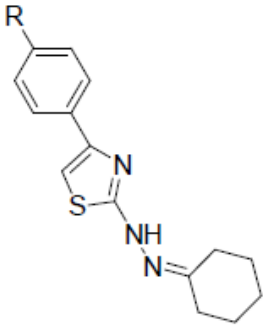


Figure (11)
11a & b[
11a, R=OCH_3, 11b, R=Br

Yamawaki *et al* in 2008 synthesized a new series of 7_-[2-(2-amino-5-chlorothiazol-4-yl)-2(Z)-((S)-1-carboxy ethoxyimino)acetamido] cephalesporins with siffrent pyridinium groups in c-3` situation. Among these cephalosporins, the group of 2-amino-1-(3-methylamino-propyl)-1H-imidazo-[4,5-b]-pyridiniumin c-3` situation (figure 12) have strongest and most balanced anti- bacterial activities against p. aeruginos and the other Gram negative pathogens [14].

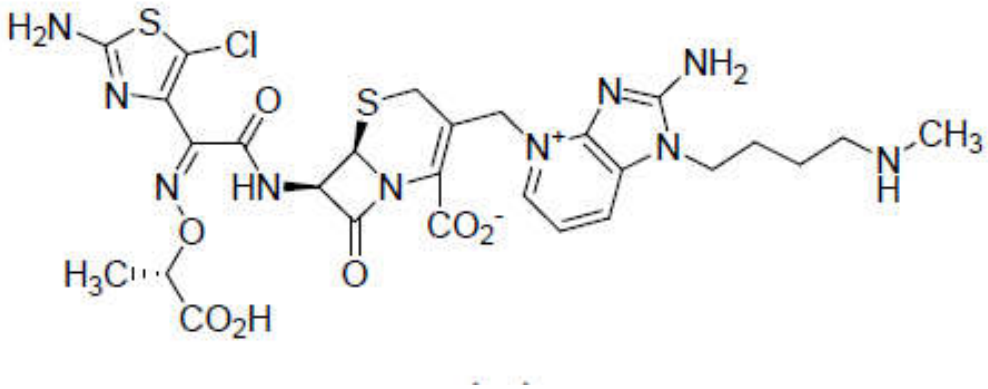


Figure 12

Khalil *et al* (2009) combined some of the 3-oxopropiononitrile and thioamide derivatives for synthesizing the new thiazol. In this regard, compound (130 had the strongest anti-bacterial activity [15].

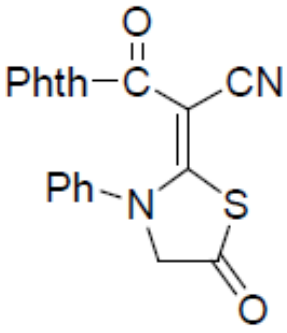


Figure (13)
Kareqoudar *et al* have reported a series of new thiazol of 4-aryl/chloroalkyl-2-(2,3,5-trichlorophenyl)-1,3- and by compressing 2,3,5-trichlorobenzenecarbothioamide with phenacylbromide establish 4-aryl-2(2,3,5-trichlorophenylidene hydrazino) -1,3-thiazoles compound with high efficiency. The result shows that (14a- d), (15 a- b) and (16a- b) have the stronger activity (16).

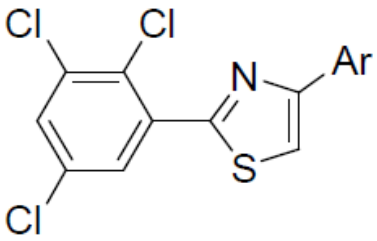


Figure (14)

14a-d[
14a, Ar=3-pyridyl, 14b, Ar=biphenyl
14c, Ar=4-NO_2 – C_6H_4, 14d, Ar= 4-Cl-C_6H_4

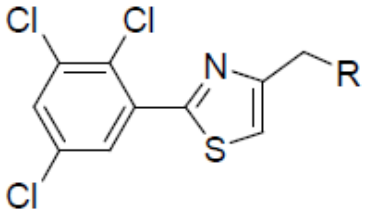


Figure (15)
15a-b[
15a, R= piperidino
15b, R= 4-mercaptopyrazoloptrimi

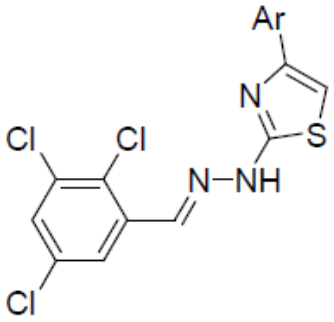


Figure (16)
16a-b[
16a, Ar=3-pyperidyl, 16b, Ar=4-No_2
Mallikrajuna *et al* synthesized a series of 4-isopropylthiazole-2-carbohydrazide analogs deviated from the combination of derivatives of ox diazole- thiazole and triazole- thiazole and their anti-bacteria, anti-fungal and anti-tuberculosis activities were examine in vitro against Mycobacterium tuberculosis H37Rv strain by using broth dilution assay method. Compound (17a- c) had the most power for anti-tuberculosis activity [17].

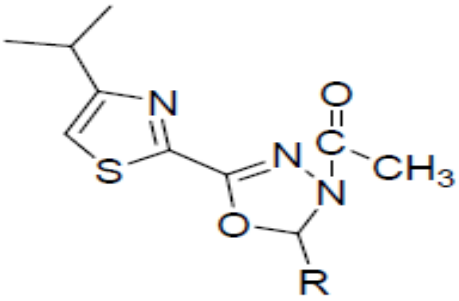


Figure (17)
17a-c[
17a, R=C_6H_5
17b, R=3, 4, 5-$(OCH_3)_3$-C_6H_2
17c, R=4-OH-C_6H_4
DWANE ET AL (28) synthesized 1-(4-(4'-chlorophenyl)-2-thiazolyl)-3-aryl-5-(2-butyl-4-chloro-1H-imidazol-5yl)-2-pyrazoline in order to test the antifungal and antibacterial activities. The results show that compound (18a- e) is stronger in view of anti-bacterial and antifungal activities (18).

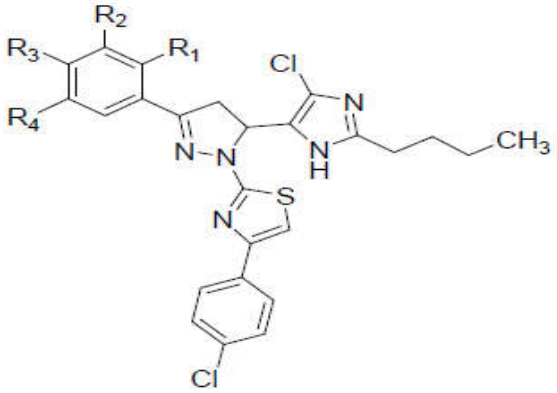


Figure (18)
18a-e[
18a, R_1=OH, R_2=I, R_3=H, R_4=Cl
18b, R_1=OH, R_2=Br, R_3=H, R_4=Cl
18c, R_1=OH, R_2=I, R_3=H, R_4=Cl
18d, R_1=OH, R_2=Br, R_3=H, R_4=Brl
18e, R_1=OH, R_2=Cl, R_3=H, R_4=Cl

Patel *et al* (2010) synthesized 2-substituted phenyl-3-[1-cyclopropyl-6-fluoro- 7-[4-(4-methoxyphenylpiperazin-1-yl]-4-oxo-1, 4-dihydroquinoline] carboxamido-1, 3-thiazolidin-4-ones; then, they have screened them for evaluating the antifungal and antibacterial activities. The results of the study shows that compound (19a- c) have the strong properties of antifungal activities while the compound (19a c) has the strongest antibacterial activity [19].

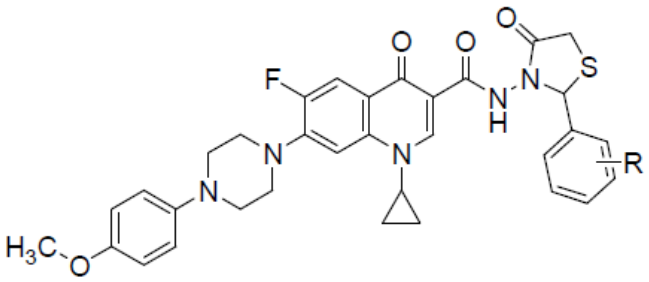


Figure (19)
19a-f[
19a, R=3-OCH_3, 19b, R=4-OH, 19c=OH
19d, R=2-NO_2, 19e, R=2-Cl, R=4-Cl
Adibpour *et al* in 2010 synthesized the several activates of 5-((3-oxoisothiazol-2(3H)-yl)methyl)-3-phenyloxazolidin-2-ones and recognized 2-(4-substituted phenyl)-3(2H)-isothiazolones replaced with 4 or 3 situation of phenyl section with different groups that some of them shows the antibacterial activities in both compounds and 3-aryl-2-oxazolidinone and 3(2H)- isothiazolones. The finding show the compound (20a- c) has stronger activity [20].

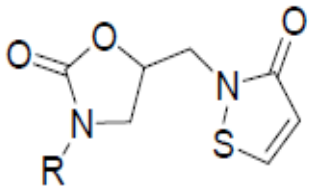


Figure (20)
20a-c[
20a, R=C_6H_5, 20b, R=4-f-C_6H_4, 20c, R=-CH-C_6H_4

Sindhu *et al* (2010) synthesized the oxovanadium (IV) complexes of Schiff (21). The complexes were monometrics and had a 1:2 stoichiometry relationship and screened compounds were screened for their antimicrobial activities [21].

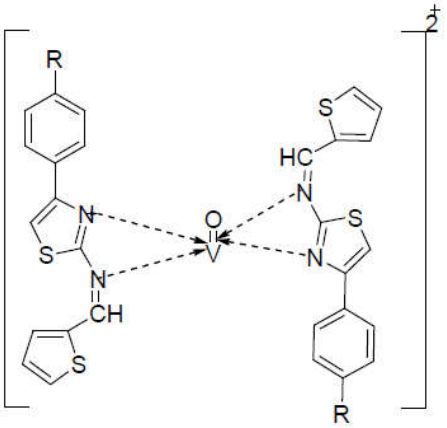


Figure (21): R=H, OH, OCH_3, NO2, Cl, Br, and CH3

Arshad *et al* in 2011 synthesized two novel series of Thoazolylcoumarin derivative and evaluated their antimicrobial activities *in vitro* against *Mycobacterium tuberculosis* and *Candida albicans*. The results showed (22a, 22b and 23) compounds are very strong for anti- inflammatory activity [22].

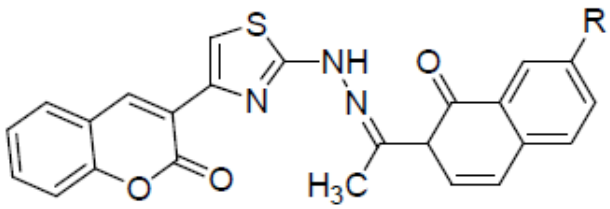


Figure (22)
22a&b[
22a, R=Br, 22b, R=OH

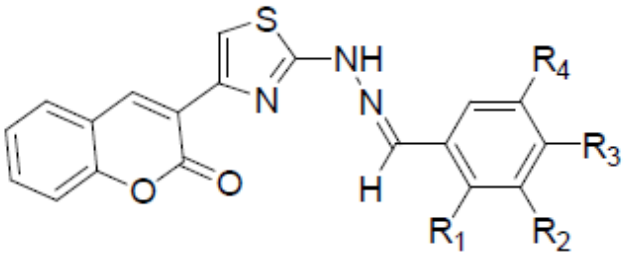


Figure (23)
23, R_1=OH, R_2=H, R_3=H, R_4=Br

Sondhi *et al* have reported the differences between N-(4-phenyl-3-(2′,3′,4′-(un)substituted phenyl)thiazol-2(3H)-ylidene)-2,4-(un)substituted acridin-9-amine and [(2,4-(un)substituted acridin-9-yl)-3-(4-phenyl-3-(2′,3′,4′-(un)substituted phenyl)thiazol-2(3H)-ylidene)]isothiourea derivatives. Then, they were screened for their anti- inflammatory and anti Kinse and analgesic activities. Among them, compounds (24) and (25) were stronger [23].

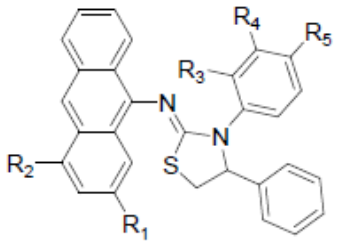


Figure (24)
24, R_1=H, R_2=OCH_3, R_3=CH_3, R_4= CH_3, R_5=H

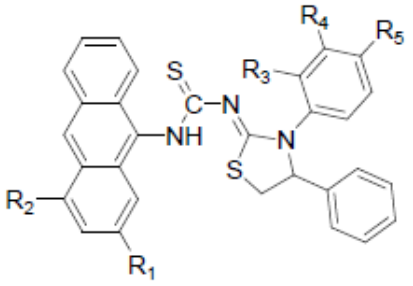


Figure (25): R_1=H, R_2=CH_3, R_3= R_4=H, R_5= CH_3

Singh *et al* synthesized a series of 3-(2'-substituted indolidene aminothiazol-4'-yl)-2-(4-chlorophenyl) indole and they were injected into the Albino rat in p.o.50 mg. kg doze for their anti- inflammatory activity against carrageenan. The most active compound was compound (26) that showed the low percentage of digestive activity and acute toxicity against Phenyl Butazone [24].

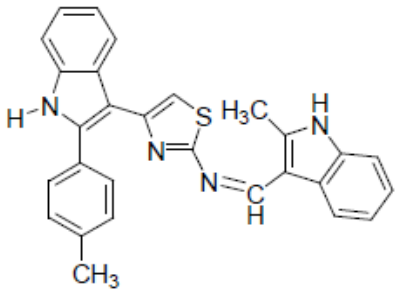


Figure (26)

Kumar *et al* in 2007 in a study synthesized a group of 3-[4'(p-chlorophenyl) thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethy]-6 bromoquinazolin-4-ones and screened them for their anti-inflammatory and analgesic activities. The compound (27) is active for both mentioned activities. They found that the existence of Thiazolidinon ring in 50 kg/mg showed a better anti-inflammatory activity than analgesic activity than the present compounds. The compounds substituted with Chloro group at second position of Phenyl ring have shown almost activity equal to inflammatory activity against standard drug phenylbutazone at 50 mg/kg.

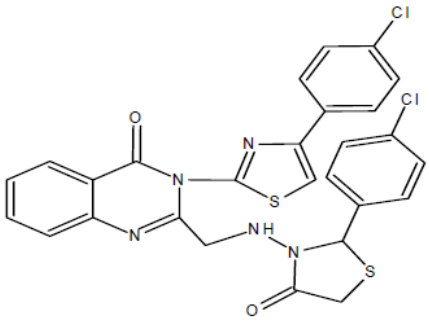


Figure (27)

Holla *et al* in 2003 in their reports have screened different series of arylaminothiazoles ،arylidene/5-aryl-2-furfurylidene hydrazinothiazoles and their antibacterial and anti-inflammatory activities. Two new artificial compounds (28) and (29) showed the inflammatory activity in comparison with ibuprofen [25].

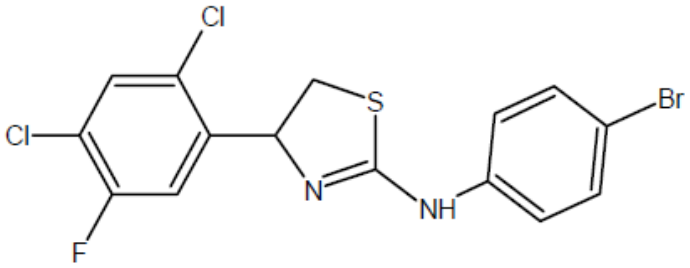


Figure (28)

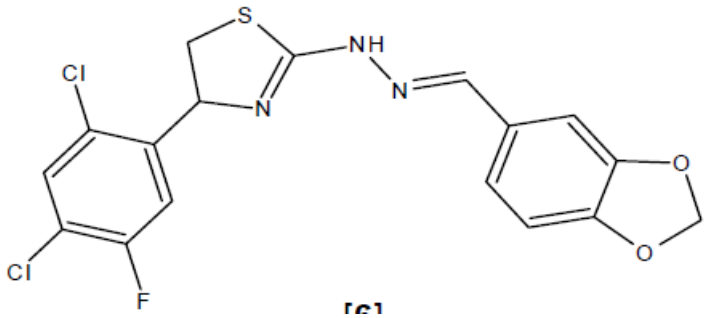
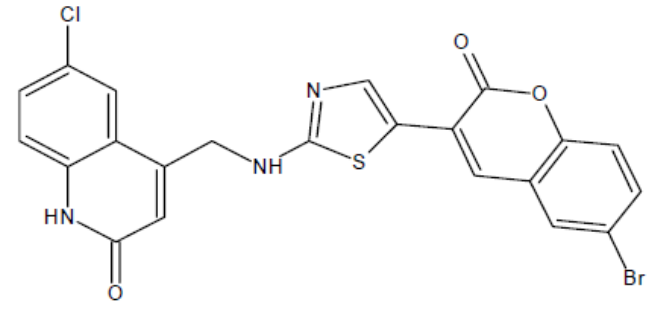


Figure (29)

Kalkhambkar *et al* in 2007 have reported triheterocyclic thiazoles that contains coumarin and (1- aza coumarin) carbostyril. The new synthesized compounds were tested in vitro for their anti-inflammatory and analgesic activities. Among the tested drugs, compounds (30) and (31) significantly prevented the entrance of acetic acid [26].



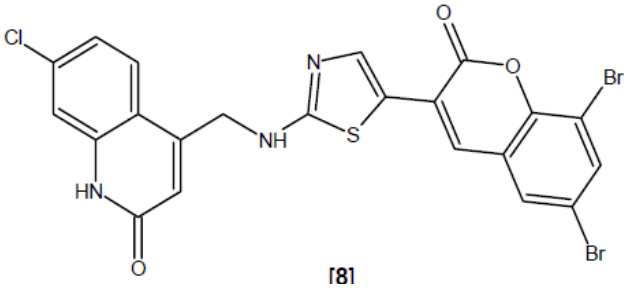


Figure (30) and (31)

Amin *et al* in 2008 have reported several new substituted coumarinyl thiazolinescoumarinyl thiazolidin-4-ones compounds and substituted chromenothiazoles and examined them for their anticonvulsant activity. Compounds (32) and (33) showed the most active of the series against PTZ induced seizures [27].

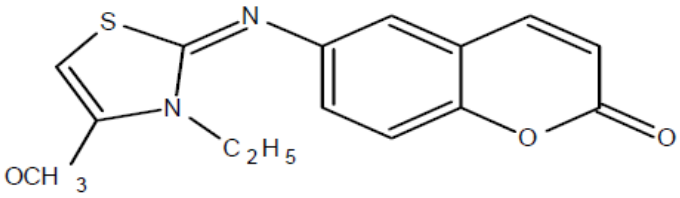


Figure (32)

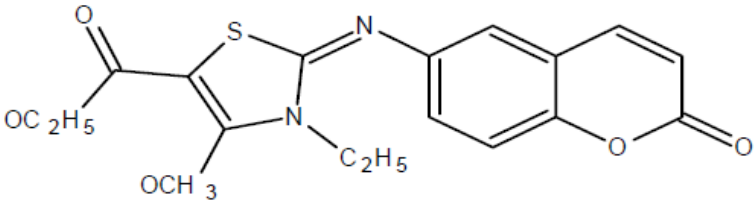


Figure (33)

Dawood *et al* have reported a series of novel synthesized compounds and examined them for their anti-inflammatory and anticonvulsant activities. The new synthesized compounds (34) had the anticonvulsant and anti- inflammatory activity with the same action mechanism of selective COX-2 inhibitors. In view of structure- activity relationship, the anti- inflammatory activity of 5- acetyl-1, 3, 4-thiadiazole derivatives were shown to be high activity than the substituted Phenyl derivatives and decreases with substitution in order of H> 4-CH_3>4-CL. furthermore, the anti- inflammatory effect of thiazolidine derivatives is higher than the acetyl derivatives and chlorinated ester derivate of 1, 3, 4- thiadiazole is effective than its non-chlorinated derivate [28].

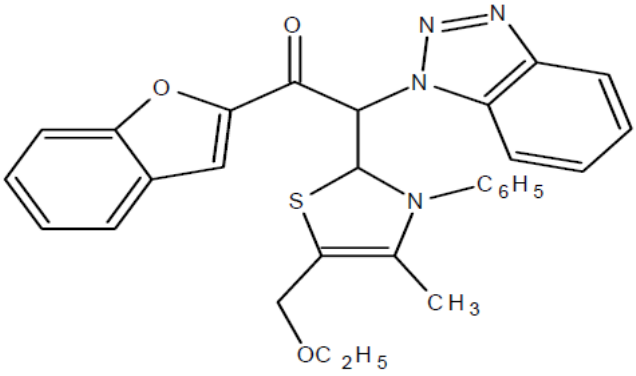


Figure (34)

Satoh *et al* found that 4-fluoro-N-[4-[6-(isopropylamino)-pyrimidin-4-yl]-1,3-thiazol-2-yl]-N-methyl benzamide compounds called a strong indicator, mGluR1, as a detector PET have high ability in mGluR1 performance in human [29].

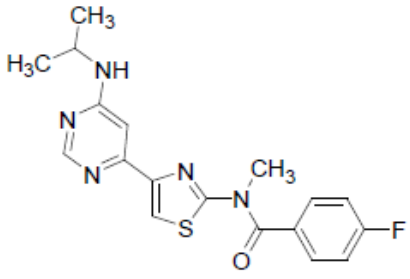


Figure (34)

Agarwal *et al* in 2006 synthesized a set of 5-[(Nsubstitutedbenzylidenylimino) amino]-2-oxo /thiobarbituric acids and screened them in vitro for sever toxicity and anticonvulsant studies. The results showed that compounds [35a &b] are stronger [30].

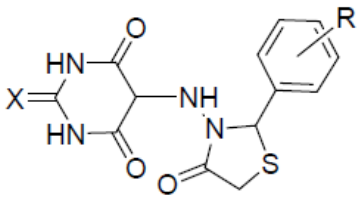


Figure (35)
35a &b[
35a, X=S, R=4-OCH_3
35b, X=S, R=3-OCH_3, 4-OH

Siddiqui *et al* in 2011 synthesized a series of thiazol derivatives with substituted thiazol and investigated for their anticonvulsant activity in vitro. They found that compounds (36a-c) had stronger anticonvulsant activity [31].

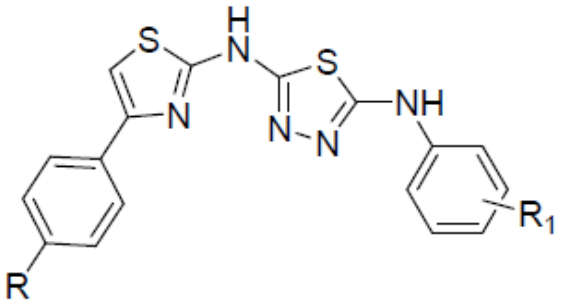


Figure (36)
36a-c[
36a, R=Br, R=OCH_3
36b, R=NO_2, R=4-CH_3
36c, R=NO_2, R=4-OCH_3

Siddiqui *et al* [32] 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 and screened them for their anticonvulsant activity by using MES and scPTZ in vitro. The findings represented the compounds 37a and 37b have significant anticonvulsant activity.

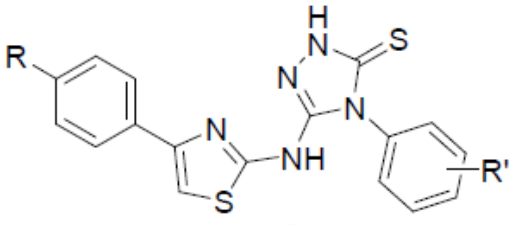


Figure (37)
37a & b[
37a, R=Cl, R'=Br
37b, R=4-CH_3, R'=2-CH_3

CONCLUSION

THIAZOLES can easily be synthesized and represented many changes with different reaction states in different positions sue to their high reactivity. In addition, the benefits of synthetic, biological and

pharmaceutical activities were expected from diazoles derivatives. Therefore, more studies needs to perform in alteration field and thiazols derivatives with aim of requirement in future.

REFERENCES

1. Barzegar, M ((2013). The synthesis of several antimicrobial potential derived from hydrazine and Thiazole Thiazole ring Htrvksyl NAD, The DVM. Kerman University of Medical Sciences and Health Services, School of Pharmacy and Pharmaceutical Sciences, Pharmaceutics Research Center.
2. M. Fontecave, S. Ollagnier-de-Choudens, E. Mulliez. (2003). Chem. Rev., 12, 2149.
3. SanthoshPenta, RajeswarRaoVedula, (2012), RETRACTED: A facile one-pot synthesis of thiazoles and thiazolyl-pyrazole derivatives via multicomponent approach, organic communication, 5:3, 143-149.
4. Siddiqui, Nadeem, Arshad, M. Faiz, Ahsan, Waquar, Alam, M. Shamsher, (2009), Thiazoles: A Valuable Insight into the Recent Advances and Biological Activities, 1, 136-143.
5. Marcus Vinícius Nora de Souza, (2005), Synthesis and biological activity of natural thiazoles: An important class of heterocyclic compounds, Journal of Sulfur Chemistry, 26:4-5, 429-449.
6. A. Kleemann, J. Engel. (2001).Pharmaceutical Substances, 4th Edition.
7. Quiroga J, Hernandez P, Insuasty B, Abonia R, Cobo J, Sanchez A, Nogueras M, Low JN. (2002). Control of the Reaction Between 2-Aminobenzothiazoles and Mannich Bases: Synthesis of pyrido[2,1-*b*][1,3] benzothiazoles*versus* [1,3]benzothiazolo[2,3-b]quinazolines. J ChemSoc Perkin Trans1. 4:555-559
8. Koufaki M, Kiziridi C, Nikoludaki F, Alexis MN. (2007). Design and synthesis of 1,2-dithiolane derivatives and evaluation of their neuroprotective activity. Bioorg Med ChemLett; 17:4223-4227.
9. Shih MH, Ying KF. (2004). Syntheses and evaluation of antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives. Bioorg Med Chem. 12:4633-4643.
10. Pandeya SN, Sriram D, Nath G, DeClerq E. (1999). Synthesis, antibacterial, antifungal and anti-HIV activities of Schiff and Mannich bases derived from isatin derivatives and N-[4-(4'-chlorophenyl) thiazol-2-yl] thiosemicarbazide. Eur J Pharm Sci. 9:25-31.
11. Shiradkar MR, Murahari KK, Gangadasu HR, Suresh T, Kalyan CA, Panchal D, Kaur R, Burange P, Ghogare J, Mokale V, Raut M. (2007). Synthesis of new S-derivatives of clubbed triazole as anti-*Mycobacterium tuberculosis* agents. Bioorg Med Chem. 15:3997-4008.
12. Vicini P, Geronikaki A, Anastasia K, Incerti M, Zani F. (2006).Synthesis and antimicrobial activity of novel 2-thiazolyl imino-5-arylidene-4-thiazolidinones. Bioorg Med Chem. 14:3859-3864.
13. Abdel-Wahab BF, Abdel-Aziz HA, Ahmed EM. (2009). Synthesis and antimicrobial evaluation of 1- (benzofuran-2-yl)-4-nitro-3-arylbutan-1-ones and 3-(benzofuran-2-yl)-4,5-dihydro-5-aryl-1-[4-(aryl)- 1,3-thiazol-2-yl]-1H-pyrazoles. Eur J Med Chem. 44: 2632-2635.
14. Yamawaki K, Nomura T, Yasukata T, Tanimoto N, Uotani K, Miwa H, Yamano Y, Takeda K, Nishitani Y. (2008).A novel series of parenteral cephalosporins exhibiting potent activities against both Pseudomonas aeruginosa and other Gram-negative pathogens. Part 2: Synthesis and structure–activity relationships. Bioorg Med Chem ; 16: 1632-1647.
15. Khalil AM, Berghot MA, Gouda MA. (2009). Synthesis and antibacterial activity of some new thiazole and thiophene derivatives. Eur J Med Chem; 44: 4434-4440.
16. Karegoudar P, Karthikeyan MS, Prasad DJ, Mahalinga M, Holla BS, Kumari NS. (2008). Synthesis of some novel 2,4-disubstituted thiazoles as possible antimicrobial agents. Eur J Med Chem; 43: 261-267.
17. Mallikarjuna BP, Sastry BS, Kumar GVS, Prasad RY, Chandrashekar SM, Sathisha K. (2009).Synthesis of new 4-isopropylthiazole hydrazide analogs and some derived clubbed triazole, oxadiazole ring systems-A novel class of potential antibacterial, antifungal and antitubercular agents. Eur J Med Chem; 44: 4739-4746.
18. Dawane BS, Konda SG, Mandawad GG, Shaikh BM. Poly(ethylene glycol) (PEG-400) as an alternative reaction solvent for the synthesis of some new 1-(4- (4-chlorophenyl)-2-thiazolyl)-3-aryl-5-(2-butyl-4- chloro-1H-imidazol-5yl)-2 pyrazolines and their in vitro antimicrobial evaluation. Eur J Med Chem 2010; 45: 387-392.
19. Patel NB and Patel SD. Synthesis and antimicrobial study of fluoroquinolone based thiazolidinones. Med Chem Res 2010; 19: 757–770.
20. Adibpour N, Khalaj A, Rajabalian S. (2010). Synthesis and antibacterial activity of isothiazolyloxazolidinones and analogous 3(2H)-isothiazolones. Eur J Med Chem; 45: 19-24.
21. Sindhu Y, Athira CJ, Sujamol MS, (2010). Mohanan K. Synthesis, characterization and antibacterial studies of oxavanadium (IV) complexs with thiazole derived Schiff Bases. Phosphorus Sulphur and Silicon; 185: 1955-1963.
22. Arshad A, Osman H, Bagiey MC, Lan CK, Mohamad S, Safirah A, Zahariluddin M. (2011). Synthesis and antimicrobial properties of some new thiazolyl coumarin derivatives. Eur J Med Chem; 1-7.
23. Sondhi SM, Singh N, Lahoti AM, Bajaj K, Kumar A, Lozach O, Meijer L. (2005). Synthesis of acridinylthiazolino derivatives and their evaluation for antiinflammatory, analgesic and kinase inhibition activities. Bioorg Med Chem ,13: 4291-4299
24. Singh N, Bhati SK, Kumar A. (2008). Thiazolyl/oxazolylformazanylindoles as potent anti-inflammatory agents. Eur J Med Chem; 43: 2597-2609.
25. Holla BS, Malini KV, Rao BS, Sarojini BK, Kumari NS. (2003). Synthesis of some new 2, 4- disubstituted thiazoles as possible antibacterial and anti-inflammatory agent. Eur J Med Chem. 38:313-318.
26. Kalkhambkar RG, Kulkarni GM, Shivkumar H, Rao NR. (2007). Synthesis of novel triheterocyclic thiazoles as anti-inflammatory and analgesic agents. Eur J Med Chem. 2007; 42:1272-1276.

27. Amin KM, Rahman ADE, Al-Eryani YA. (2008). Synthesis and preliminary evaluation of some substituted coumarins as anticonvulsant agents. Bioorg Med Chem. 16:5377-5388.
28. Dawood KM, Gawad HA, Rageb EA, Ellithey M, Mohamed HA. (2006). Synthesis, anticonvulsant, and anti-inflammatory evaluation of some new benzotriazole and benzofuran-based heterocycles. Bioorg Med Chem.; 14:3672–3680
29. Satoh A, Nagatomi Y, Hirata Y, Ito S, Suzuki G, Kimura T, Maehara S, Hikichi H, Satow A, Hata M, Ohta H, Kawamoto H. (2009). Discovery and in vitro and in vivo profiles of 4-fluoro-N-[4-[6- (isopropylamino)pyrimidin-4-yl]-1,3-thiazol-2-yl]- N-methylbenzamide as novel class of an orally active metabotropic glutamate receptor 1 (mGluR1) antagonist. Bioorg Med Chem ; 19: 5464-5468.
30. Agarwal A, Lata S, Saxena KK, Srivastava VK, Kumar A. (2006). Synthesis and anticonvulsant activity of some potential thiazolidinonyl 2-oxo/thiobarbituric acids. Eur J Med Chem; 41: 1223–1229.
31. Siddiqui N and Ahsan W. (2011). Synthesis, anticonvulsant and toxicity screening of thiazolyl–thiadiazole derivatives. Med Chem Res; 20: 261–268.
32. Siddiqui N and Ahsan W. (2010). Triazole incorporated thiazoles as a new class of anticonvulsants: Design, synthesis and in vivo screening. Eur J Med Chem; 45: 1536–1543.