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Biological Activity Profile of Thiazolidinone Scaffolds Linked to Bioactive Thiazoles: A Review

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ABSTRACT

Thiazolidinones have been explored in both academia and pharmaceutical industry for their wide spectrum of biological applications which include activity against streptomyces species, anti-convulsant, hypoglycemic, antihypertensive agents and therefore, they are useful molecules for drug research and organic chemistry. Thiazolidinone derivatives containing thiazole ring system are also found to possess pharmacological activities such as anticancer, antimalarial, tuberculostatic, anticonvulsant, anti-HIV activity and CNS stimulants. Extensive research in the synthesis and biological evaluation of thiazolidinone substituted heterocycles is well documented and hence, attracted the interest of organic chemist. Therefore, the objective of this review to highlight the biological properties of thiazolidinone derivatives bearing thiazole ring system. The introductory paragraph highlights the significance of the thiazolidinone moiety and is followed by an overview of thiazole heterocycle. In the next section pharmacological properties of thiazolidinone linked thiazole derivatives has been described

Key words: 4-Thiazolidinone, Thiazole, Heterocycles, Biological Activity

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INTRODUCTION

Presence of heterocycles in bioactive natural products has recently received considerable attention as precursors in the field of drugs and pharmaceuticals. Especially, biological significance of nitrogen and sulphur containing heterocyclic compounds made them important synthetic targets and always drawn the attention of chemist over the years. The thiazolidinone and thiazole derivatives are the most extensively investigated classes of five membered heterocycles containing nitrogen and sulfur heteroatoms.

Thiazolidinone is a very versatile scaffold and has been considered as a magic moiety (wonder nucleus). Thiazolidinones are classified as saturated form of thiazole have an sulfur atom at position 1, an nitrogen atom at position 3 and a carbonyl group at position 2, 4, or 5. But the greatest difference in structure and properties is exerted by the 1,3-thiazolidin-4-ones. Therefore, its derivatives are the subject of renowned interest and its presence in penicillin was the first recognition of its occurrence in nature.¹ Several thiazolidinone fused thiazole molecules has been reported to possess important biological activities such as anti-inflammatory,² antitubercular,³ antimicrobial,⁴ antidiabetic,⁵ antiviral⁶ and anti-HIV.⁷



Thiazolidinone

Thiazole or 1,3-thiazole ring system is another privileged heterocyclic scaffold, also recognized as a biologically important motif employed for the preparation of variety of natural products and bioactive compounds and are proved to be clinically useful agents against different kinds of disease. Therefore, the chemistry and pharmacology of thiazoles are of great interest from both a medicinal and a synthetic perspective because its derivatives are associated with diverse biological activities *viz.* antimicrobial,⁸ antibacterial,⁹ antifungal,¹⁰ anti-inflammatory¹¹ and antitubercular.¹² Structures of biologically active thiazolidinone and thiazole nucleus are shown in Figure. 1.

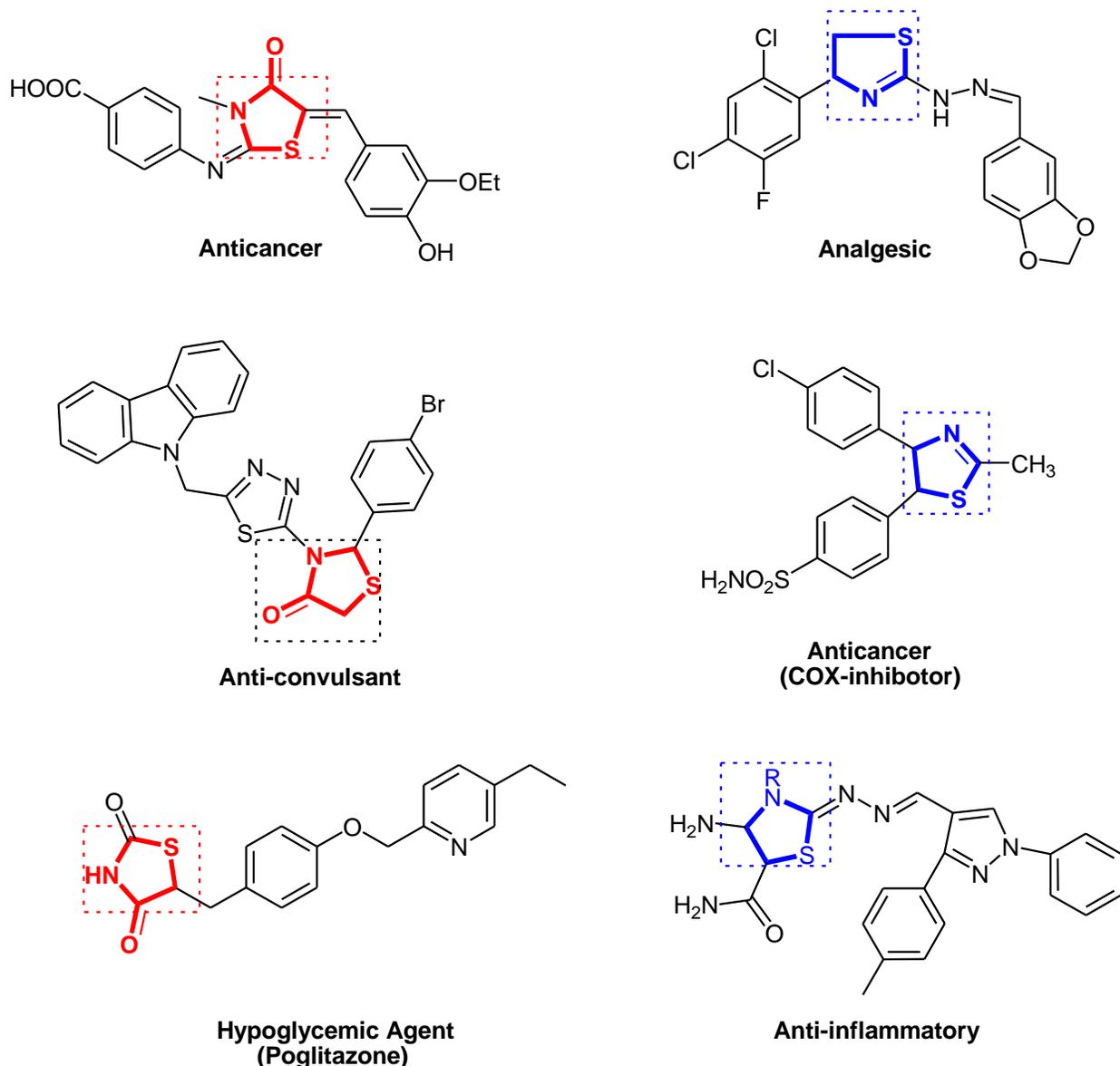


Figure 1: Biologically active thiazolidinone and thiazole derivatives

Motivated by the above reported observations which shows diversity in the biological response profile of thiazolidinones and thiazoles, it was considered worthwhile to present a review in which emphasis is given on various pharmacological properties associated with substituted thiazolidinones incorporating thiazole scaffolds as a single framework.

Thiazolidinone Substituted Thiazole Derivatives As Biologically Active Agents

Due to their importance in pharmaceutical utilities, the synthesis of various thiazolidinone derivatives is of considerable interest. The presence of thiazole core in bioactive active molecules has also stimulated the interest in thiazole chemistry. Therefore, to enhance the biological properties and stability of structure, new methodologies have been developed for the construction of thiazolidinone derivatives encompassing with other heterocycle ring.

Altintas et al.¹⁴ synthesized Mannich bases of various 2,5-disubstituted-4-thiazolidinones derivatives of mannich base was synthesized and investigated for antimicrobial activities by Altintas et al.¹⁴. They concluded that the synthesized molecules are inactive against *Proteus Mirabilis*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, *Staphylococcus epidermidis*, *Shigella flexneri*, *Pseudomonas aeruginosa*, *Escherchia coli* and *Staphylococcus aureus* but found to have antifungal activity against *Trichophyton rubrum*, *Microsporium canis*, *Candida albicans*, *Trichophyton mentagrophytes*, and *Microsporium gypseum*. Results revealed that piperidine and morpholine moieties attached at the 5th position of the thiazolidinone ring **5** (Figure 4) was found to be more active against *Trichophyton rubrum*, *Microsporium canis* and *Trichophyton mentagrophytes* and *Trichophyton rubrum*, *Microsporium canis*, *Microsporium gypseum*, *Trichophyton mentagrophytes* respectively indicating that the presence of ethyl groups caused potential antifungal activity. Also the introduction of dimethylamine and 2,5-pyrrolidindione moieties **6** (Figure 4) led to enhanced activity.

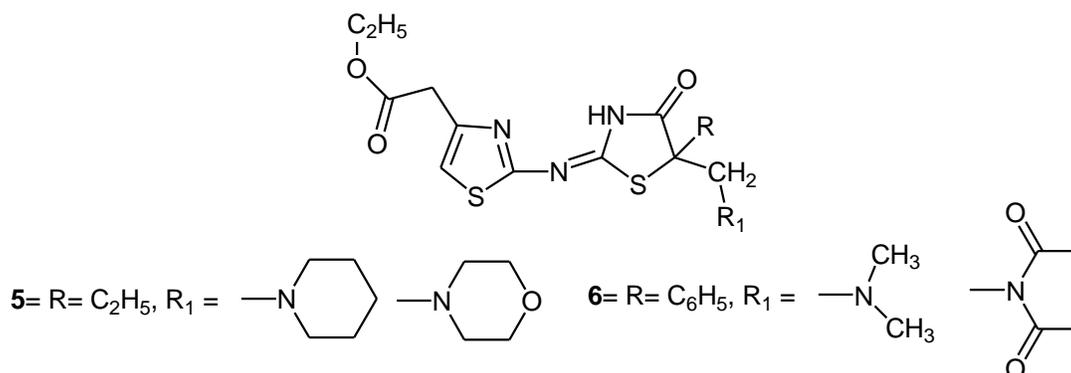


Figure 4: Mannich base substituted thiazolidinones 5 and 6 as potent antifungal agent

Desai and co-workers had synthesized 2-(aryl)-3-[2-(benzothiazolylthio)-acetamidyl]-4-oxo-thiazolidinones derivatives **7** (Figure 5) and all these products were evaluated for their antibacterial activity against *Escherchia coli* (Gram +ve), *Staphylococcus aureus* and *Bacillus subtilis* (Gram +ve).¹⁵

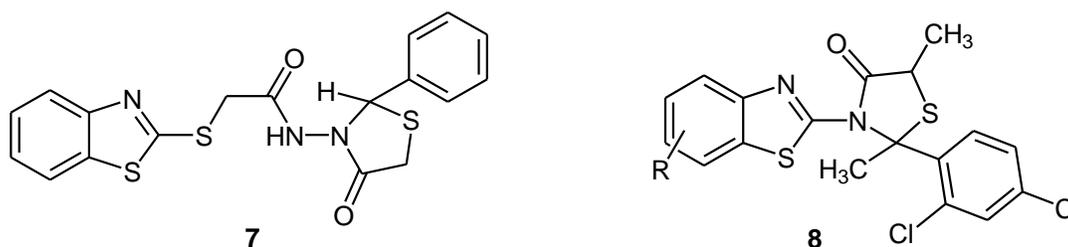


Figure 5 Antibacterial benzothiazole-substituted-oxo-thiazolidinone 7 and benzothiazole-substituted-2,5-dimethyl-thiazolidinone 8

Novel 2-(2'',4''-dichloro-phenyl)-2,5-dimethyl-3-benzothiazol-substituted-thiazolidinone derivatives were screened for their antifungal activity and antibacterial activity against *Candida albicans* and *Bacillus substilis*, *Escherchia coli*, *Staphylococcus aureus* respectively by Desai et al.¹⁶ Most of the thiazolidinone derivatives **8** (Figure 5) revealed comparable activity against tested strains by taking penicillin and tetracycline as reference drug.

Synthesis and antifungal evaluation of novel derivatives of 4-thiazolidinones had been performed by Patel et al.¹⁷ Compounds were examined for antifungal activity against *Penicillium Expansum*, *Botrydepladia Thiobromine*, *Nigrospora Sp.* and *Trichothesium Sp.* The comparison of the antifungal activity of the compound **9** (Figure 6) with sulphanilamide shows that these compounds have almost similar activity. A variety of new thiazolyl-thiazolidinylbenzothiazole derivatives were synthesized by Singh et al.¹⁸ but none of the compounds was found to have antibacterial activity where as compounds were potent for insecticidal activity. They noted that the presence of electron withdrawing *p*-OCH₃ group at phenyl ring **10** (Figure 6) was shown to increase insecticidal activity.

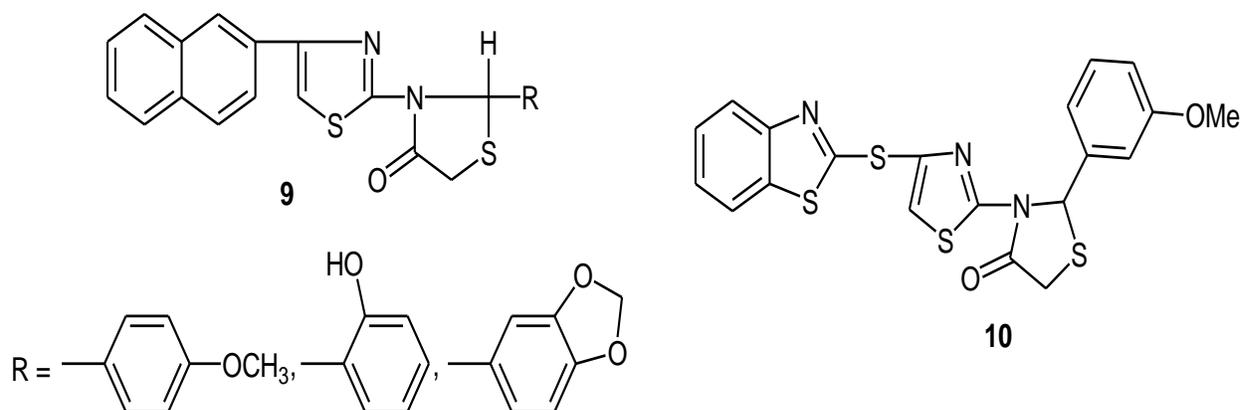


Figure 6: Activity of thiazole-substituted thiazolidinones 9 and antibacterial activity of thiazolyl-thiazolidinylbenzothiazole derivatives 10

A variety of new thiazolyl-thiazolidinylbenzothiazole derivatives were synthesized by Singh et al.¹⁸ but none of the compounds was found to have antibacterial activity where as compounds were potent for insecticidal activity. They noted that the presence of electron withdrawing *p*-OCH₃ group at phenyl ring **10** (Figure 6) was shown to increase insecticidal activity.

Vicini et al.¹⁹ synthesized series of substituted 5-arylidene derivatives. Compound **11** (Figure 7) in which chloro group is present at the para position of the aryl group was shown to improve antibacterial activity and hydrophilic hydroxyl or methoxy group or nitro group seemed to be a non-profitable structural feature.

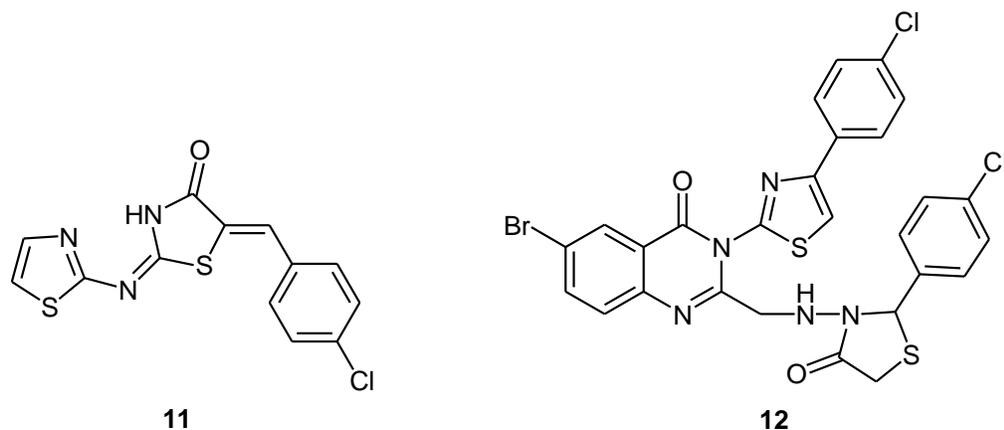


Figure 7:Thiazolidinone substituted 5-arylidene derivatives (antibacterial activity) 11 and bromoquinazoline substituted thiazolidinones (analgesic and anti-inflammatory activity) 12

Kumar *et al.*²⁰ reported the synthesis of bromoquinazoline substituted thiazolidinones. Among all synthesized molecules thiazolidinone **12** (Figure 7) showed highest analgesic and anti-inflammatory activity.

Synthesis and skeletal muscle relaxant, analgesic, anti-inflammatory, CNS depressant evaluation of 2-substituted-arylthiazolidine-4-ones has been described by Gurupadayya *et al.*²¹ Their results revealed that among different substituted-arylthiazolidineones compound **13** and **14** were found to possess maximum anti-inflammatory against standard diclofenac and significant muscle relaxant activity respectively Compound **15** exhibited higher CNS depressant and analgesic activity than the standard diazepam and pentazocine respectively (Figure 8)

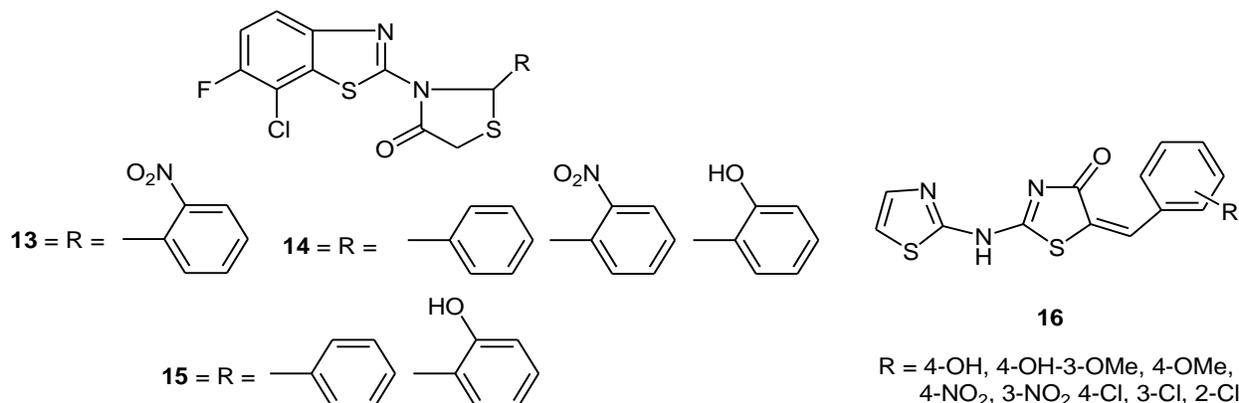
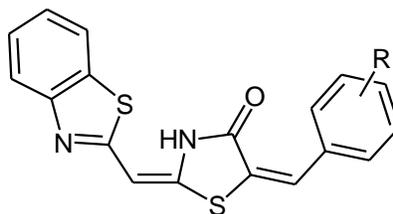


Figure 8: Benzothiazol-substituted-arylthiazolidinones 13-15 and thiazole-phenylidene substituted thiazolidinones 16

New thiazole-phenylidene substituted thiazolidinones **16** as an anti-inflammatory agent possessing dual cyclooxygenase/lipoxygenase (COX/LOX) inhibition were discovered by Geronikaki *et al.*²². Using PASS (Prediction of Activity Spectra for Substances), authors summarized that compounds

with *m*-OCH₃, *p*-OH and *m*-NO₂ substitution exhibited the highest anti-inflammatory activity, also have the best LOX inhibition (Figure 8).

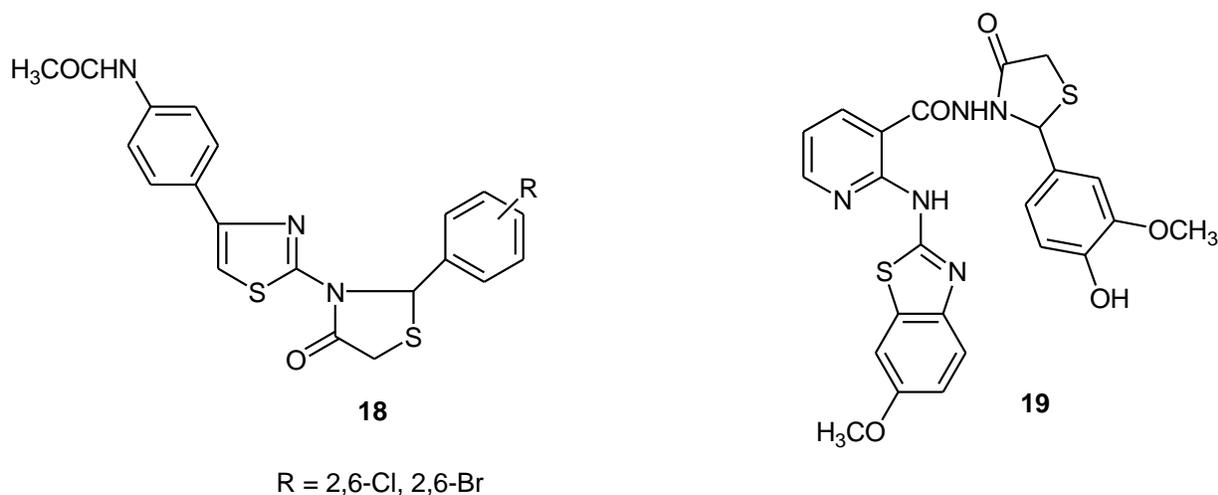
Vicini *et al.*²³ has synthesized 5-benzylidene substituted thiazolyl-thiazolidinones **17** (Figure 9) and evaluated their antimicrobial activity. Benzothiazole substituted compounds showed antibacterial property when screened against penicillin-resistant strains, *Staphylococci* and *Bacilli*, whereas some of the tested benzisothiazoles are selective against *Bacilli*.

**17**

R = 4-OH, 4-OCH₃, 3-OCH₃-4-OH, 2-NO₂, 3-NO₂, 4-NO₂, 2-Cl, 3-Cl, 4-Cl

Figure 9: 5-Benzylidene substituted thiazolyl-thiazolidinones as antimicrobial agent

Several N-2-[(2R)-2-(substitutedphenyl)-4-oxo-1-thiazolidinyl]-4-(3-acetanilido)thiazoles have been synthesized by Indu *et al.*²⁴ and concluded that when compound **18** (Figure 10) tested against bacterial strains like *Proteus vulgaris*, *Staphylococcus aureus* and *Escherichia coli*, it showed better antibacterial activity. Ampicillin and ciprofloxacin were used as a reference drugs. Benzothiazole substituted thiazolidinones derivatives have been synthesized and evaluated for antimicrobial activity towards bacterial and fungicidal strains by Patel *et al.*²⁵ Compound **19** (Figure 10) revealed significant antibacterial activity against *Escherichia coli* compared to the reference drug ampicillin.

**18****19**

R = 2,6-Cl, 2,6-Br

Figure 10: Antibacterial (3-acetanilido)thiazole-substituted thiazolidinones 18 and antimicrobial benzothiazole substituted thiazolidinones 19

Synthesis and antimicrobial activity of 4-adamantyl-2-thiazolylimino-5-arylidene-4-thiazolidinones **20** (Figure 11) against bacterial strains (gram positive and gram negative bacteria) were studied by Omar *et al.*²⁶. They reported that the most active compound had *p*-OH and 3,5-OCH₃ group on arylidene moiety. Results revealed that *m*-Cl, *p*-NO₂, *m*-NO₂, *m*-OCH₃ and 3,5-OCH₃-4-OH substituted compound showed higher activity against tested strains whereas replacement of hydroxyl group with methoxy in 4th position usually decreased activity.

Anticancer activity of benzothiazole-thioxo substituted thiazolidinone **21** with average log GI₅₀ value as -5.38 and log TGI values as -4.45 has been reported by Havrylyuk *et al.*²⁷. Further, they described that presence of different substituents on thiazolidinone ring affects the potency and presence of substituted halo aryl group enhances the anticancer activity.

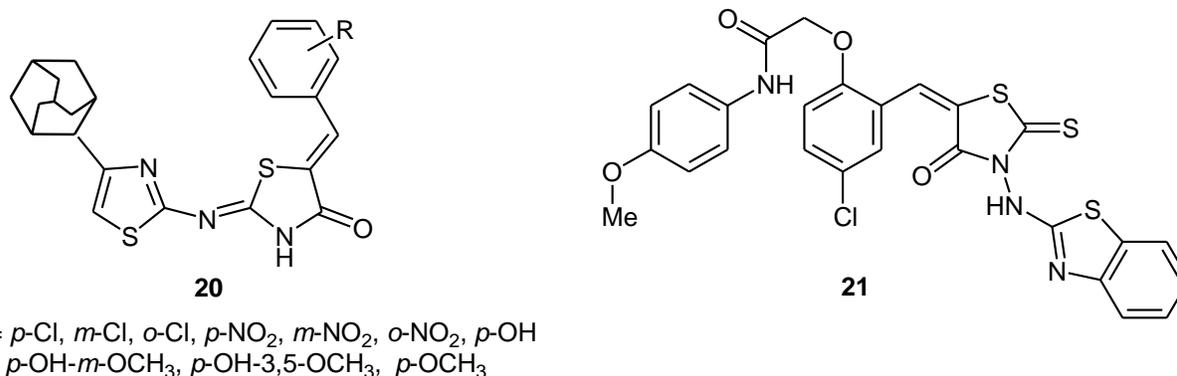


Figure 11: 4-Adamantyl-2-thiazolylimino-5-arylidene-4-thiazolidinones **20 and Benzothiazole-thioxo substituted thiazolidinone **21****

Kini *et al.*²⁸ have synthesized and explored the hypoglycemic activity of coumarino substituted thiazol-thiazolidinones derivatives **22** (Figure 12) and concluded that the electro-negativity of halo groups present at *meta* and *para* positions responsible for the variation in hypoglycemic activity

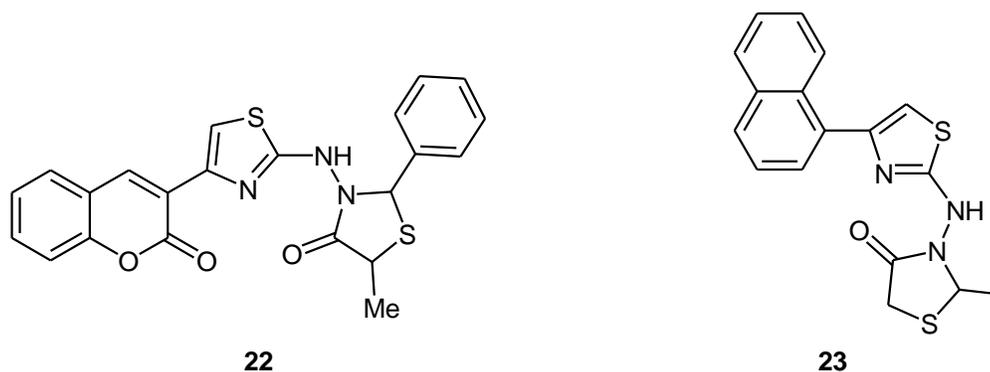
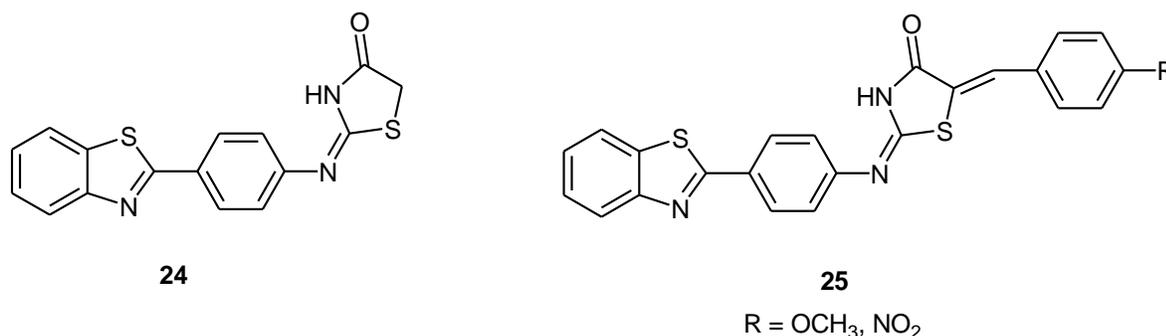


Figure 12: Hypoglycemic activity of thiazolidinones derivatives of coumarino **22 and thiazolidinone derivatives of naphthy-thiazolyl **23****

Ahmed *et al.*²⁹ synthesized thiazolidinone derivatives substituted with naphthyl-thiazolyl group **23** (Figure 12) as antihyperglycemic agents. The synthesized compounds, displayed moderate to good antidiabetic activity against standard drug pioglitazone. The study was aimed at evaluating the anticonvulsant effect of compounds on mice.

Abdelgawad *et al.*³⁰ reported the synthesis and cytotoxic activity of substituted thiazolidinones and their 5-arylidene derivatives.



Figure

13: Anticancer benzothiazole thiazolidinones 24 and their 5-arylidene derivatives 25

Compound **24** (Figure 13) was identified as the most potent one since it displayed the most prominent cytotoxicity with IC₅₀ value 79 nM and 83 nM against human breast MCF7 and liver HEPG2 cancer cell lines respectively. It was further concluded that the compound **25** (Figure 13) found to be the most active candidates against liver HEPG2 cancer cell line with IC₅₀ value 0.026 nM due to presence of methoxy groups on aryl ring. *p*-Nitro substituted benzylidene-thiazolidinone derivative of benzothiazole also found to be more potent against MCF7 and HEPG2 cell lines which displayed IC₅₀ = 36 and 48 nM respectively.

Abdelazeem *et al.*³¹ synthesized a series of diphenylthiazole substituted thiazolidinone derivatives **26** bearing a sulfonamide group and reported for their anticancer activity against five cancer cell lines; HCT-116 (human colon cancer), Caco-2 (human colon carcinoma), MCF-7 (human breast carcinoma), DU-145 (human prostate carcinoma, epithelial-like cell line) and PC-

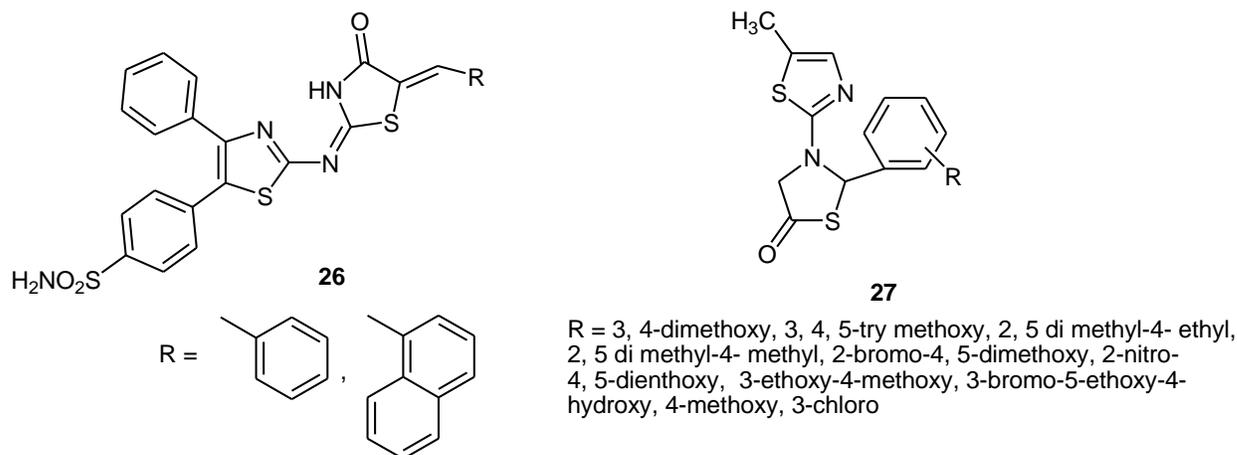


Figure 14: Diphenylthiazole substituted thiazolidinone derivatives 26 (Anticancer). Thiazolidinone derivatives of thiazol 27 (Antibacterial)

3 (human Prostate Carcinoma). Compound **26** (Figure 14) displayed a good COX-2 growth inhibitory comparable to that of celecoxib against a panel of cancer cell lines showing half maximal inhibitory concentrations (IC_{50}) between 8.88 and 19.25 μ M. Thiazolidinone derivatives of thiazol **27** (Figure 14) was found to exhibit selective and effective inhibition of a wide spectrum of bacterial strains (*Salmonella typhimurium*, *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus*) as compared to standard drugs like Amoxicillin and Ciprofloxacin. Furthermore, studies have revealed that the presence of electron-donating group encourages the activity profile.³²

Samadhiya and co-workers³³ had synthesized series of N-[2-{2-(substitutedphenyl)-4-oxo-5-(substitutedbenzylidene)-1,3-thiazolidine}-iminoethyl]-2-amino-5-nitrothiazole **28** (Figure 15) and screened there *in vitro* antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis* and *Escherichia coli*. Synthesized compounds were also examined towards *Candida albicans*, *Aspergillus niger* and *Aspergillus flavus* for antifungal activity against. Streptomycin for antibacterial and griseofulvin for antifungal activity were used as standards. Compounds were also screened against M. tuberculosis (H37_{Rv}) strain and variation in antitubercular activity was observed due to substituted aromatic ring of thiazolidinones. Isoniazid and rifampicin were taken as standard antitubercular drugs. They found that the presence of electron-withdrawing

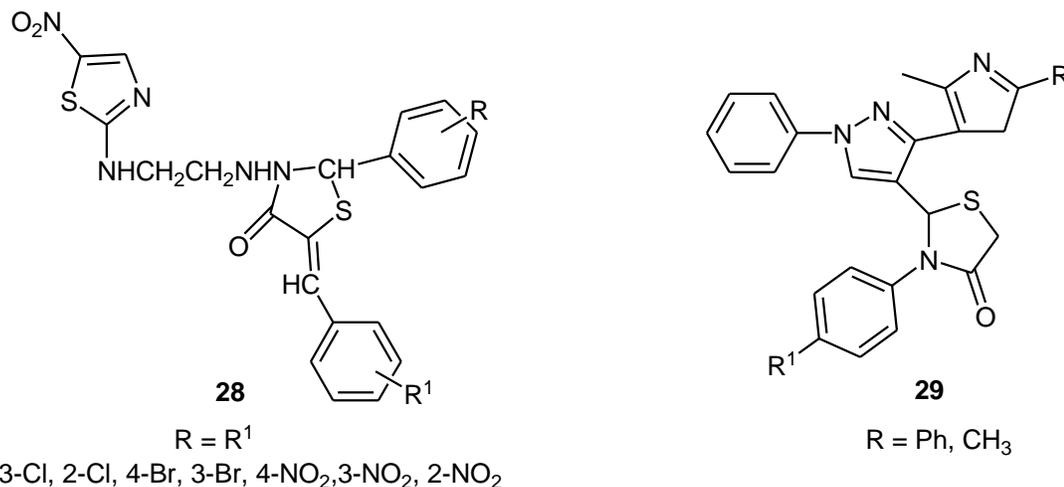


Figure 15: 2-amino-5-nitrothiazole-thiazolidinones 28 (antibacterial, antifungal and antitubercular agents) and pyrazole/thiazole substituted thiazolidinones 29 (anti-inflammatory agents)

nitro group at *ortho*, *para* and *meta* position phenyl ring augments the activity profile than chloro or bromo group containing compounds. It is interesting to point out that the chloro and bromo derivatives also have higher activity than other tested compound. The anti-inflammatory properties of novel pyrazole and thiazole substituted thiazolidinones **29** (Figure 15) were studied using carrageenan induced mice paw edema method and compared to reference drug Celecoxib. Khillare *et al.*³⁴ noted that the presence of halogen groups on aryl ring possessed more potent anti-inflammatory activity.

Haroun *et al.*³⁵ reported novel thiazolidine-thiazole substituted esters **30** (Figure 16) and screened them against variety of pathogens for their antibacterial activity (four Gram (+) bacteria; *Bacillus cereus* clinical isolate, *Micrococcus flavus*, *Staphylococcus aureus*, *Listeria monocytogenes* and four Gram (-) bacteria; *Escherichia coli*, *Enterobacter cloacae* human isolate, *Pseudomonas aeruginosa*, *Salmonella typhimurium*) and antifungal activity (*Aspergillus fumigates*, *Aspergillus versicolor*, *Aspergillus ochraceus*, *Aspergillus niger*, *Trichoderma viride*, *Penicillium funiculosum*, *Penicillium ochrochloron* and *Candida albicans*). The results showed that the tested compounds possessed good antibacterial and antifungal activities compared to standard drugs ampicillin, streptomycin for antibacterial activity and ketoconazole, bifonazole for antifungal activity. They reported that the 4-bromo and 3-nitro derivatives showed best antibacterial activity against *Bacillus cereus* and best antifungal activity against *Trichoderma viride* respectively.

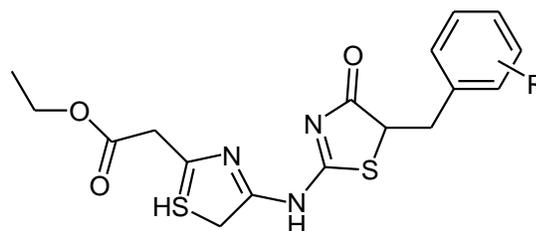
**30**R = 4-Br, 3-NO₂

Figure 16: 4-oxothiazolidinone derivatives of ethyl acetates 30 as antibacterial and antifungal agents

CONCLUSION

The literature reveals that 4-thiazolidinone containing thiazole motifs are important compounds of biological and medicinal interest. The anticancer and anti HIV activities are the most encouraging activities for the pharmacists. Besides this some of the new biological activities associated with thiazolidinone linked thiazole scaffolds has been explored such as anticonvulsant, agonistic and inhibitory activity. From these observations importance of this nucleus is highlighted along with the wide spectra of biological/pharmacological properties. Specific MIC values has also been incorporated which may provide valuable information for the further design and development of more active biological agents through various modifications and derivatizations. We would like to apologize to those scientists whose work may not have appeared in this review either due to the limited description of the review or oversight.

REFERENCES

1. Jain AK, Vaidya, A, Ravichandran V, Kashaw SK, Agrawal RK. Recent developments and biological activities of thiazolidinone derivatives: A review *Bioorg Med Chem* 2012; 20: 3378-3395.
2. Geronikaki AA, Lagunin AA, Hadjipavlou-Litina DI, Eleftheriou PT, Filimonov DA, Poroikov VV, Alam I, Saxena AK. Computer-aided discovery of anti-inflammatory thiazolidinones with dual cyclooxygenase/lipoxygenase inhibition. *J Med Chem* 2008; 51: 1601-1609.
3. Parekh HH, Parikh KA, Parikh AR. Synthesis of some 4-thiazolidinone derivatives as antitubercular agents. *J Sci Islm Rep Iran* 2004; 15 (2): 143-148.
4. Lokhandwala SR, Desai KR. Novel organophosphorus compounds as potential antimicrobial agents. *Phosphorus, Sulfur and Silicon Relat Elem* 2008; 183: 1264-1271.

5. Murugan R, Anbazhagan S, Narayanan SS. Synthesis and in vivo antidiabetic activity of novel dispiropyrrolidines through [3 +2] cycloaddition reactions with thiazolidinedione and rhodanine derivatives Eur J Med Chem 2009; 44: 3272-3279.
6. Terzioglu N, Karali N, Gursoy A, Pannecouque C, Leysen P, Paeshuyse J, Neyts J, Clercq ED. Synthesis and primary antiviral activity evaluation of 3-hydrazono-5-nitro-2-indolinone derivatives. Arkivoc 2006; 1: 109-118.
7. (a). Balzarini J, Orzeszko-Krzesinska B, Maurin JK, Orzeszko A. Synthesis and anti-HIV studies of 2- and 3- adamantyl-substituted thiazolidin-4-ones. Eur J Med Chem 2009; 44: 303-311; (b). Ravichandran V, Mourya VK, Agrawal RK Prediction of anti-HIV activity of 1,3-thiazolidin-4-ones: QSAR approach. Dig J Nanomater Bios 2008; 3 (1): 19-31; (c). Rawal RK, Kumar A, Siddiqi MI, Katti SB. Molecular docking studies on 4-thiazolidinones as HIV-1 RT inhibitors. J Mol Model 2007; 13: 155-161; (d). Rawal RK, Tripathi R, Katti SB, Pannecouque C, Clercq ED. Design, synthesis and evaluation of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones as anti-HIV agents. Bioorg Med Chem 2007; 15: 1725-1731.
8. Gouda MA, Berghot MA, El-Ghani GE, Abd Khalil AM. Synthesis and antimicrobial activities of some new thiazole and pyrazole derivatives based on 4,5,6,7-tetrahydrobenzothiophene moiety. Eur J Med Chem 2010; 45: 1338-1345.
9. (a). Bharti SK, Nath G, Tilak R, Singh SK. Synthesis, anti-bacterial and anti-fungal activities of some novel Schiff bases containing 2,4-disubstituted thiazole ring. Eur J Med Chem 2010; 45: 651-660; (b) Khalil AM, Berghot MA, Gouda MA. Synthesis and antibacterial activity of some new thiazole and thiophene derivatives. Eur J Med Chem 2009; 44: 4434-4440.
10. Jaish L, Srivastava SK. Synthesis and antimicrobial activity of some new N-methyl piperazinythiadiazoles and their azetidinones. J Sci Ind Res 2001; 60: 331-335.
11. Giri RS, Thaker HM, Giordano T, Williams J, Rogers D, Sudersanam V, Vasu KK. Design, synthesis and characterization of novel 2-(2,4-disubstituted-thiazole-5-yl)-3-aryl-3H-quinazoline-4-one derivatives as inhibitors of NF- κ B and AP-1 mediated transcription activation and as potential anti-inflammatory agents. Eur J Med Chem 2009; 44: 2184-2189.
12. Shiradkar M, Venkata G, Kumar S, Dasai V, Tatikonda S, Chakravarthy AK, Shah R. Clubbed triazoles: A novel approach to antitubercular drugs. Eur J Med Chem 2007; 42: 807-816.

13. Liu HL, Li Z, Anthonsen T. Synthesis and fungicidal activity of 2-imino-3-(4-arylthiazol-2-yl)-thiazolidin-4-ones and their 5-arylidene derivatives. *Molecules* 2000; 5: 1055-1061.
14. Altintas H, Ates O, Birteksoz S, Otuk G, Uzun M, Satana D. Synthesis of mannich bases of some 2,5-disubstituted 4-thiazolidinones and evaluation of their antimicrobial activities. *Turk J Chem* 2005; 29: 425-435.
15. Desai KG, Raval JP, Desai KR. Neat reaction technology for the synthesis of 4-oxo-thiazolidines derived from 2-SH-benzothiazole and antimicrobial screening of some synthesized 4-thiazolidinones. *J Iran Chem Soc* 2006; 3: 233-241.
16. Desai KR, Mistry K. Microwave assisted synthesis of nitrogen and sulphur containing heterocyclic compounds and their pharmacological evaluation. *Ind J Chem* 2006; 45B: 1762-1766.
17. Patel KH, Mehta AG. Synthesis and antifungal activity of azetidinone and thiazolidinones derivatives of 2-amino-6-(2-naphthalenyl)thiazolo[3,2-d]thiadiazole. *E-J Chem* 2006; 3(4): 267-273.
18. Singh T, Srivastava VK, Saxena KK, Goel SL, Kumar A. Synthesis of new thiazolylthiazolidinylbenzothiazoles and thiazolylazetidinybenzothiazoles as potential insecticidal, antifungal and antibacterial agents. *Arch Pharm Chem Life Sci* 2006; 339: 466-472.
19. Vicini P, Geronikaki A, Anastasia K, Incerti M, Zani F. Synthesis and antimicrobial activity of novel 2-thiazolylimino-5-arylidene-4-thiazolidinones. *Bioorg Med Chem* 2006; 14: 3859-3864.
20. Kumar A, Rajput CS, Bhati SK. Synthesis of 3-[4'-(p-chloro phenyl) thiazol-2'-yl]-2[(substituted azetidinone/thiazolidinone) -amino methyl]-6-bromo quinazolin-4-ones. *Bioorg Med Chem* 2007; 15: 3089-3096.
21. Gurupadayya BM, Gopal M, Padmashali B, Manohara YN. Synthesis and pharmacological evaluation of azetidin-2-ones and thiazolidin-4-ones encompassing benzothiazole. *Indian J Pharm Sci* 2008; 70(5): 572-577.
22. Geronikaki AA, Lagunin AA, Hadjipavlou-Litina DI, Eleftheriou PT, Filimonov DA, Poroikov VV, Alam I, Saxena AK. Computer-aided discovery of anti-inflammatory thiazolidinones with dual cyclooxygenase/lipoxygenase inhibition. *J Med Chem* 2008; 51: 1601-1609.
23. Vicini P, Geronikaki A, Incerti M, Zani F, Dearden J, Hewitt M. 2-Heteroarylimino-5-benzylidene-4-thiazolidinones analogues of 2-thiazolylimino-5-benzylidene-4-

- thiazolidinones with antimicrobial activity: Synthesis and structure–activity relationship. *Bioorg Med Chem* 2008; 16: 3714-3724.
24. Singh I, Kaur H, Kumar S, Lata S, Kumar A, Kumar A. Synthesis and antibacterial activity of 3-chloro 4-(substitutedphenyl)azetidinyloxy/thiazolidinonyl-4-(3-acetanilido) oxa/thiazoles. *Int J of Pharm Sci Res* 2010; 1(2): 148-168.
25. Patel NB, Shaikh FM. Synthesis and antimicrobial activity of new 4-thiazolidinone derivatives containing 2-amino-6-methoxybenzothiazole. *Saudi Pharm J* 2010; 18: 129-136.
26. Omar K, Geronikaki A, Zoumpoulakis P, Camoutsis C, Sokovic M, Ciric A, Glamoclija J. Novel 4-thiazolidinone derivatives as potential antifungal and antibacterial drugs. *Bioorg Med Chem* 2010; 18: 426-432.
27. Havrylyuk D, Mosula L, Zimenkovsky B, Vasyleno O, Gzella A, Lesyk R. Synthesis and anticancer activity evaluation of 4-thiazolidinones containing benzothiazole moiety. *Eur J Med Chem* 2010; 45: 5012-5021.
28. Kini D, Ghate M. Synthesis and oral hypoglycemic activity of 3-[5'-methyl-2'-aryl-3'-(thiazole-2''-yl amino) thiazolidin-4'-one] coumarin derivatives. *E-J Chem* 2011; 8: 386-390.
29. Ahmed O, Salahuddin M, Vinutha K, Sharma P. Design, Synthesis and biological evaluation of some novel substituted thiazolidinone derivatives as potent antihyperglycemic agents. *Inter J Pharm Res Sch* 2013; 2(1):166-173.
30. Abdelgawad MA, Belal A, Ahmed OM. Synthesis, molecular docking studies and cytotoxic screening of certain novel thiazolidinone derivatives substituted with benzothiazole or benzoxazole. *J Chem Pharm Res* 2013; 5(2): 318-327.
31. Abdelazeem AH, Gouda AM, Omar HA, Tolba MF. Design, synthesis and biological evaluation of novel diphenylthiazole-based cyclooxygenase inhibitors as potential anticancer agents. *Bioorg Chem* 2014; 57: 132-141.
32. Patel VG, Goswami TK, Bhatt AR. Synthesis and biological activity of some new thiazole based thiazolidinones. *J Chem Pharm Res* 2014; 6(6): 2760-2764.
33. Samadhiya P, Sharma R, Srivastava SK, Srivastava SD. Synthesis and biological evaluation of 4-thiazolidinone derivatives as antitubercular and antimicrobial agents. *Arab J Chem* 2014; 7: 657-665.

34. Khillare LD, Bhosle MR, Deshmukh AR, Mane RA. Synthesis and anti-inflammatory evaluation of new pyrazoles bearing biodynamic thiazole and thiazolidinone scaffolds. *Med Chem Res* 2015; 24: 1380-1386.
35. Haroun M, Tratat1 C, Tsolaki E, Geronikaki A. Thiazole-based thiazolidinones as potent antimicrobial agents. Design, synthesis and biological evaluation. *Combinatorial Chemistry & High Throughput Screening* 2016; 19: 51-57.

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