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Biolgical Activities of Thiazolidine – A Review

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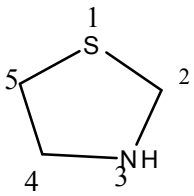
Abstract: Article is based on the different pharmacological aspects of thiazolidine ring. From the last decade a lot of work is going on the thiazolidine ring. Scientist had developed a lot of new compound related to this moiety. They have screened them for different pharmacological activities to get a molecule which have good pharmacological activity with least adverse effects.
The thiazolidine is not only synthetically important scaffold but also possesses a wide range of promising biological activities. Some thiazolidine derivatives have better activity than standard drugs and could become a new drug for the market in future.
This thiazolidine has shown its importance as antimicrobial, anti-inflammatory, anticonvulsant, antimalarial, analgesic, anti-HIV and anticancer agent.
Keywords- Thiazolidine, anticancer, anti-inflammatory, Biological activities, Future aspect

Introduction

Thiazolidines are a class of hetrocyclic organic compounds having a 5 membered saturated ring with a thio ether group at 1 position and an amine group in the 3 position. It is sulfur analogue of oxazolidine. Thiazolidines may be synthesized by a condensation reaction between a thiol and an aldehyde or ketone. It is a reversible reaction. Therefore many thiazolidines are labile towards hydrolysis in aqueous solution. Hydrolysis of the thiazolidine generates the thiol and an aldehyde from which it was synthesized [1].



❖ Among the synthesized compounds, compound **[I]** showed the most favorable antimicrobial activity.

Physical Properties of Thiazolidine

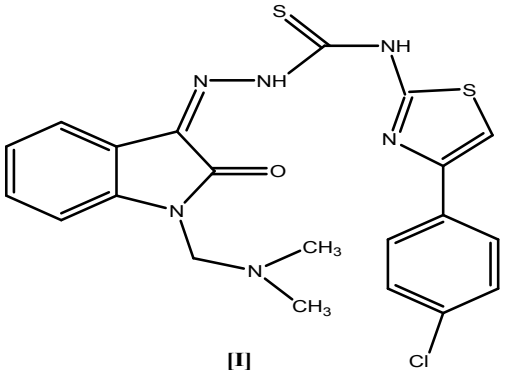
The physical properties of thiazolidine are:

Melting Point	326.69 [K]
Log $_p$	0.46
Molecular Formula	C_3H_7NS
Molecular Weight	89.16
$_p$H Value	> 6
R_F Value	0.45

Biological Activities of Thiazolidine Derivatives

Antimicrobial activity

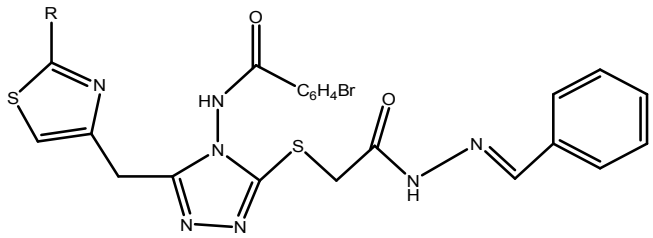
❖ Pandeya *et al.* **[2]** prepared a series of Schiff and Mannich bases, derived from isatin derivatives and N-[4-(4'chloropheyl) thiazol-2-yl] thio semicarbazide. Antimicrobial investigation of synthesized compounds was done by agar dilution method against 28 pathogenic bacteria, 8 pathogenic fungi and anti-HIV-1 in MT-4 cells.



[I]

❖ Shiradkar *et al.* **[3]** 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 amide derivatives. These compounds were tested for their preliminary *in-vitro* antibacterial activity against *S. aureus, E. coli, P. aeroginosa* and *S. typhosa* and then were screened for antitubercular activity against *M. tuberculae H37Rv* strain by both micro dilution assay method. Compound **[II]** and **[III]** showed best activity. They revealed that the compounds showing more than 90% inhibition were obtained by S-alkylation with acetonitrile. It was noted that the cyano group did not have any role in increasing in the activity.

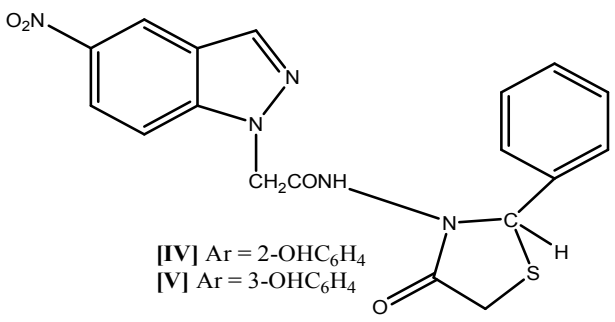
❖



[II] R= $NHCOCH_3$, Ar = 3-NO_2.C_6H_4

[III] R=$NHCOC_6H_5$ Ar = 3-NO_2.C_6H_4

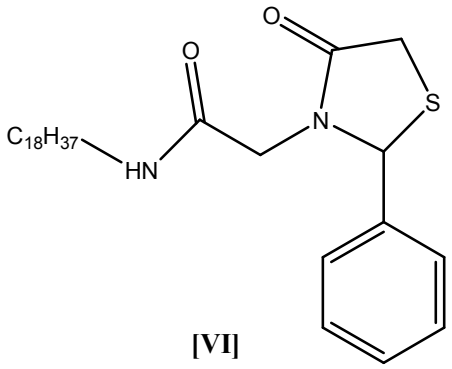
❖ Several new N-[(4-oxo-2-substituted aryl-1, 3-thiazolidine)-acetamidyl]-5-nitroindazoles were synthesized by Upadhyay A. *et al.* [**4**] from N-(arylidene amino acetamidyl)-5-nitroindazoles. The reactions were carried out by both conventional as well as microwave method. The structures of these compounds were confirmed by IR, ^{1}HNMR, ^{13}C NMR, FAB-mass spectra and also by micro analytical data. The newly synthesized compounds were evaluated for their antimicrobial activity against bacterial and fungal strains. The compound **[IV]** and **[V]** show the maximum antibacterial activity (MIC 11 and 10 mg/mL) against *Escherichia coli* and antifungal activity (MIC 9 and 8 mg/mL) against *Fusarium oxysporum*.



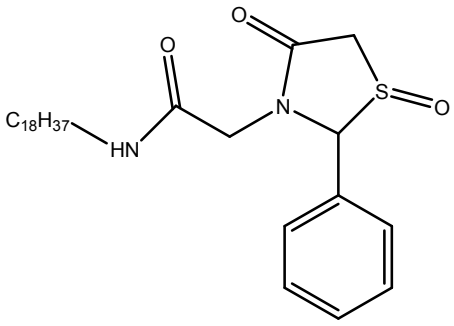
[IV] Ar = 2-OHC_6H_4
[V] Ar = 3-OHC_6H_4

Antiproliferative activity

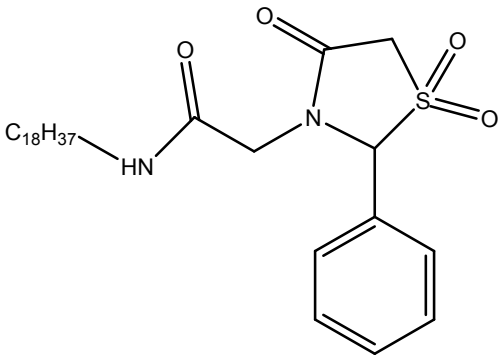
❖ Gududuru *et al.* [**5**] described the synthesis and biological evaluation of new 2-aryl-4-oxo-thiazoilidin-3-yl amides against prostate cancer cells. The antiproliferative effects of synthesized compounds were examined in five human prostate cancer cell lines (*DU-145, PC-3, LNCaP, PPC-1* and *TSU*). Three potent compounds have been identified (**VI**, **VII** and **VIII)**, which are effective in killing prostate cancer cells with improved selectivity compared to serine amide phosphates (SAPs).



[VI]



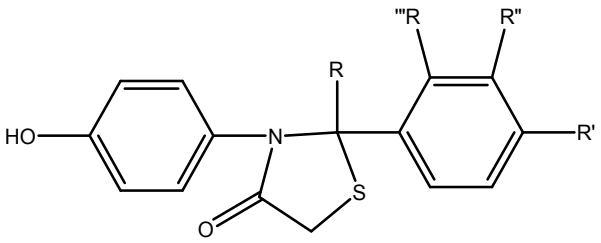
[VII]



[VIII]

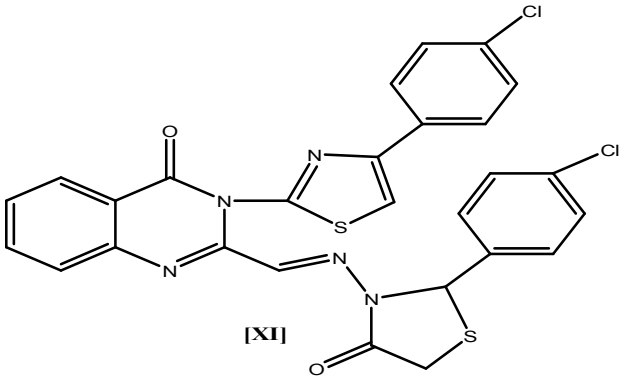
Anti-inflammatory and Analgesic activity

❖ Taranalli AD *et al.* **[6]** synthesized a series of thiazolidine-4-one derivatives from sulfanilamide and evaluated for anti-inflammatory, analgesic and anti-ulcer activity. Anti-inflammatory activity was investigated by carrageenan induced rat paw edema method and analgesic activity by acetic acid induced writhing and rat caudal immersion method. Anti-ulcer activity was investigated by pylorus ligation ulcer model. The anti-inflammatory, analgesic and antiulcer activity was performed in 100 mg/kg b.w. rats. The nimesulide was used as standard drug for comparison. The compound **[IX]** and compound **[X]** with substitution R'-CH_3 showed potential activity.



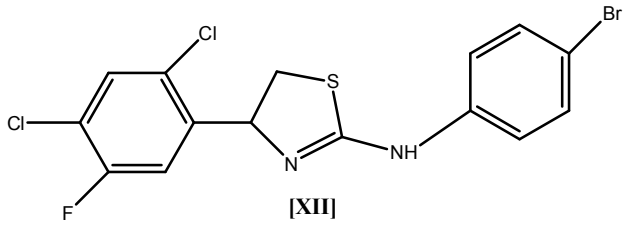
[IX] R = H, R'= H, R"= H, R'"= H
[X] R = H, R' = CH_3, R"= H, R'"= H

❖ Kumar *et al.* **[7]** synthesized a group of 3-[4'(*p*-chlorophenyl) thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethy]-6-bromoquinazolin-4-ones and screened them for anti-inflammatory and analgesic activities. Compound **[XI]** was found to be most active in both the activities. They found that the presence of thiazolidinone ring have shown much better anti-inflammatory and analgesic activity at 50 mg/kg po as compared to their parent compounds.

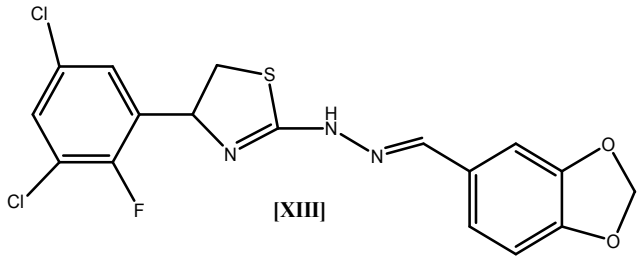


[XI]

❖ Holla *et al.* **[8]** reported the different series of arylaminothiazoles, arylidene/5-aryl-2-furfurylidene hydrazinothiazoles and screened them for their antibacterial and anti-inflammatory activities. Two of the newly synthesized compounds [**XII**] and [**XIII**] showed anti-inflammatory activity and were found to be most active.



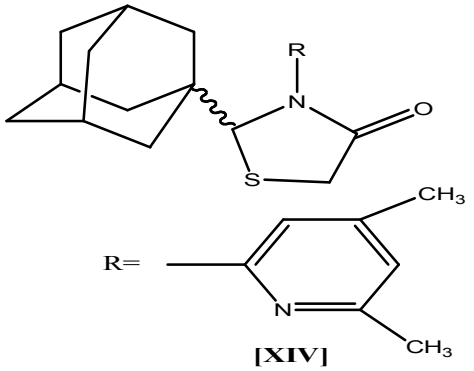
[XII]



[XIII]

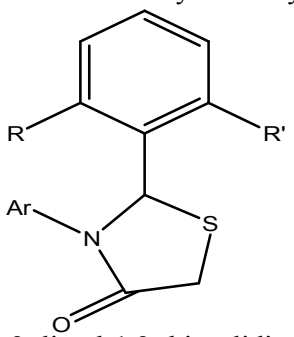
Anti-HIV activity

❖ Jan Balzarini *et al.* **[9]** synthesized a series of novel thiazolidin-4-ones bearing a lipophilic adamantyl substituent at position 2, and versatile substituents on the nitrogen atom of the thiazolidine ring, whereas several compounds exhibited a modest anti-HIV-1 activity, (+)-2-adamantan-1-yl-3-(4,6-dimethyl-pyridin-2-yl)-thiazolidin-4-one **[XIV]** was endowed with a remarkable antiviral potency (EC50 ¼ 0.35 mM). The adamantane moiety played an important role in the eventual antiviral activity of the compound. This compound behaved as a typical non-nucleoside reverse transcriptase (RT) inhibitor (NNRTI) with non-competitive inhibition against RT with respect to the substrate (Ki ¼ 12 mM).



[XIV]

❖ The anti-HIV activity of several series of 2, 3-diaryl-1, 3-thiazolidin-4-ones **[XV]** has been studied by Chavan, Y.B. *et al.* **[10, 11, 12]**. Which are reported as a new family of antiviral agents acting as NNRTIs with minimal cytotoxicity.

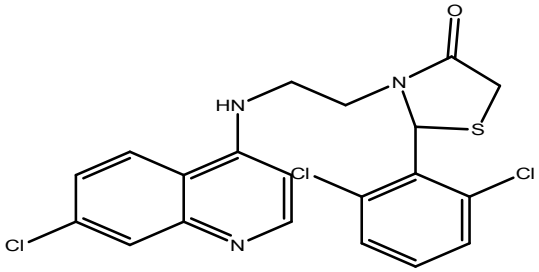


2,3-diaryl-1,3-thiazolidin-4-ones

[XV]

Antimalarial activity

❖ Solomon *et al.* **[13]** reported the synthesis of chloroquine analogues having a 1, 3-thiazolidin-4-one nucleus at the terminal side chain amino group of 4-aminoquinoline **[XVI]**. All compounds were evaluated for their antimalarial activity against *P. falciparum in-vitro* and some compounds that have shown their activity comparable to standard drug were also evaluated against *P. yoelli in-vivo*. The best compound (IC_{50} = 0.039µM) posses superior *in-vitro* activity compared to chloroquine.

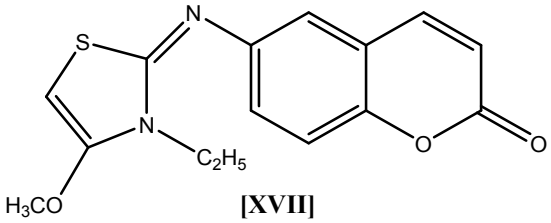


Thiazolidinone chloroquinine analogue

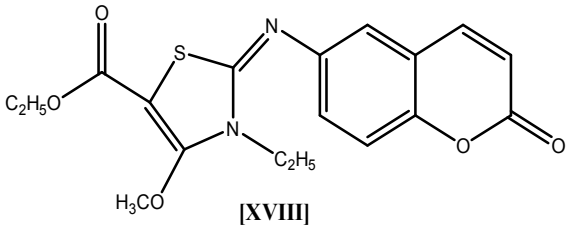
[XVI]

Anticonvulsant activity

❖ Amin *et al.* **[14]** reported some new substituted coumarinyl thiazolines, coumarinyl thiazolidin-4-ones and substituted chromenothiazoles and evaluated for the anticonvulsant activity. Compounds [**XVII**] and [**XVIII**] were the most active against PTZ induced seizures.

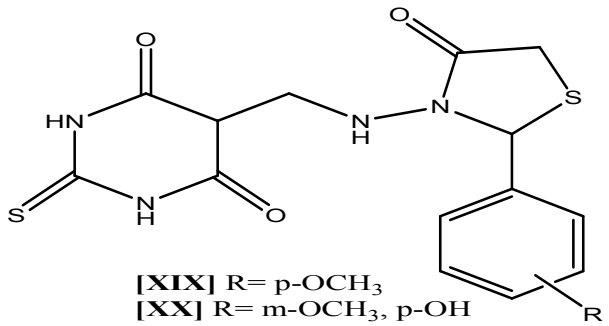


[XVII]

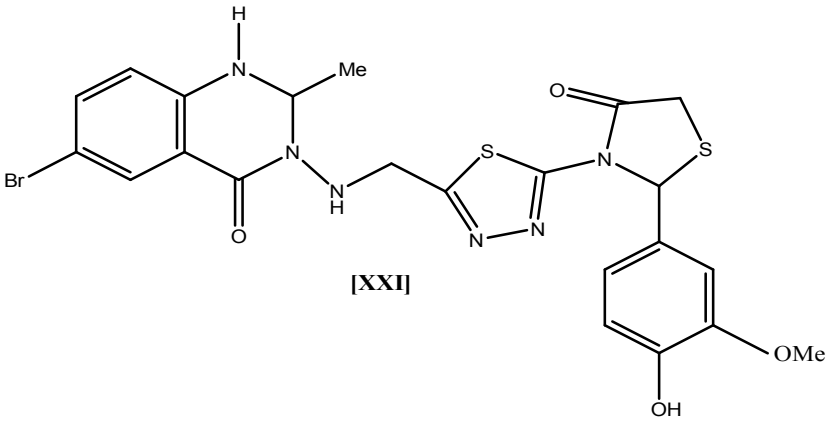


[XVIII]

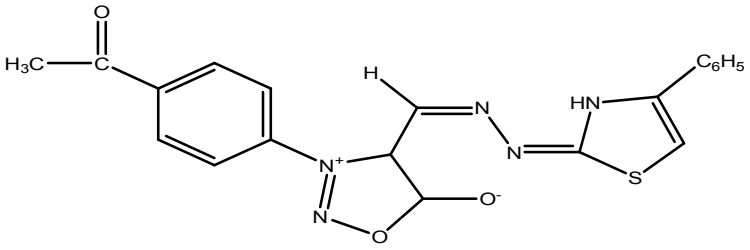
❖ Several 5-[(2-phenyl-4-oxo-thiazolidin-3-yl) amino]-2-oxo-thio barbituric acids **[XIX and XX] [15]** and 3-({4-[2-alkylphenyl)-4-oxo-1,3-thiazolidin-3-yl]-1,3,4-thiadiazol-2-yl}methylamino) -2-methyl-6-monosubstituted-quinazolin-4(3*H*)-one **[XXI] [16]** have been synthesized by Wilson Cunico *et al*. and screened *in-vivo* for their anticonvulsant activity.



[XIX] R= p-OCH_3
[XX] R= m-OCH_3, p-OH



[XXI]



[XXII]

Antioxidant activity

- Shih *et al.* **[17]** synthesized a series of sydnonyl substituted thiazolidinone and thiazoline derivatives and evaluated for their antioxidant activity. The antioxidant activity of derivatives of compound [**XXII**] have been found to exhibit the significant DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity, comparable to that of vitamin E.

Conclusion

In this article, we review the recently literature data of synthesis and biological activities of thiazolidine. The thiazolidine is not only synthetically important scaffold but also possesses a wide range of promising biological activities. Some thiazolidine derivatives have better activity than standard drugs and could become a new drug for the market in future.

Future Aspect

Future investigation could give some interesting results on substitution at various position of thiazolidine ring

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