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Research Article

Thiazole: A Review on Chemistry, Synthesis and Pharmaceutical Importance of its Derivatives

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Abstract

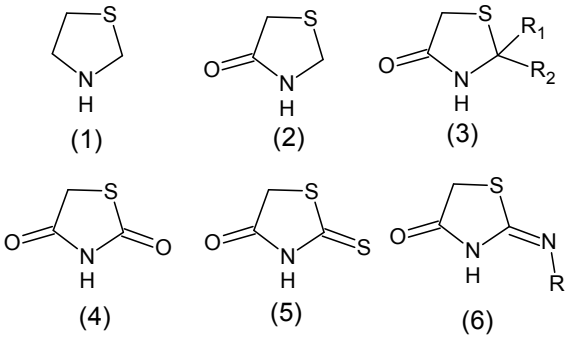
Thiazole, a unique heterocycle containing sulphur and nitrogen atoms, occupies an important place in medicinal chemistry. It is an essential core scaffold present in many natural (Vitamin B1- Thiamine) and synthetic medicinally important compounds. The versatility of thiazole nucleus demonstrated by the fact that it is an essential part of penicillin nucleus and some of its derivatives which have shown antimicrobial (sulfazole), antiretroviral (ritonavir), antifungal (abafungin), antihistaminic and antithyroid activities. The synthetic importance of thiazole derivatives, its reduced forms and condensed derivatives have been increased much by their recent applications as anticancer (tiazofurin), anthelmintic, vulcanising accelerators (mercaptobenzothiazole) and photographic sensitizers. Thiazole chemistry has developed steadily after the pioneering work of Hofmann and Hantsch. Bogert and co-workers made significant contribution to expand this field. Mills established the importance of thiazole ring in cyanine dyes which is used as photographic sensitizer. Benzothiazole, a fused derivative of thiazole have also proved its commercial value. Present review describes chemical and biological importance of thiazole and its condensed derivatives with an emphasis on recent developments.

Keyword: Pyrazole, Heterocyclic and Biological activity

Introduction and review of literature:

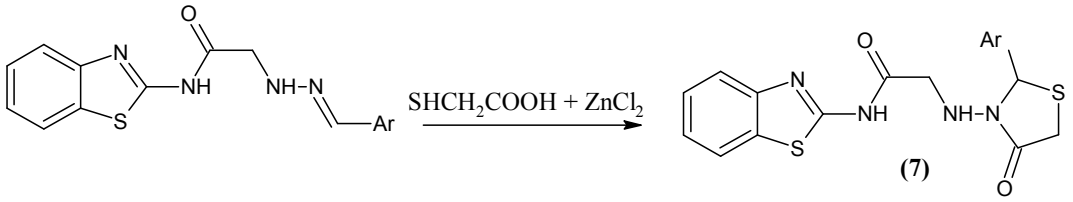
Thiazolidinones

Thiazolidinones are five membered aliphatic heterocycles containing sulphur and nitrogen at positions 1 and 3 and carbonyl group at position 4 in the same ring. It is also known as 4-oxo-thiazolidine.Thiazolidine **(1)** with a carbonyl group at 4-position is known as 4-thiazolidinone **(2)** or 4-oxo-thiazolidines **(2)**. Substituents at position 2, 3 and 5 are known and such a group can form alkyl, aryl or aryl-alkyl thiazolidinone **(3)**. The oxygen attached to C-2 would make 2,4-thiazolidinone **(4)** [1-4]. Sulphur atom attached at C-2 makes rhodanine**(5)** and imino group from 2-imino-4 thiazolidinediones**(6)**.

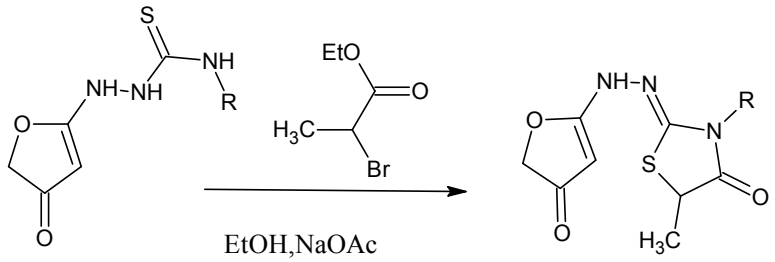


Synthetic aspects of thiazolidine

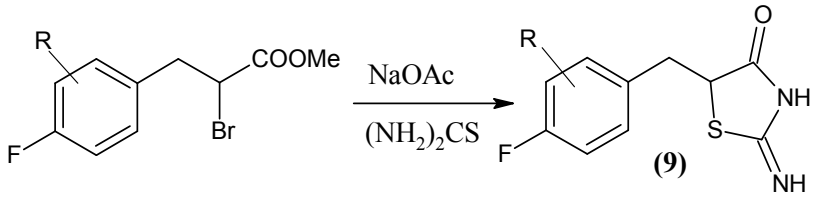
Some*N*-(1,3-benzothiazol-2-yl)-2-[(4-oxo-2-phenyl-1,3-thiazolidin-3-yl)amino]acetamide **(7)** were synthesized by Srivastava and coworkers [5]. All the compounds show antimicrobial activity.



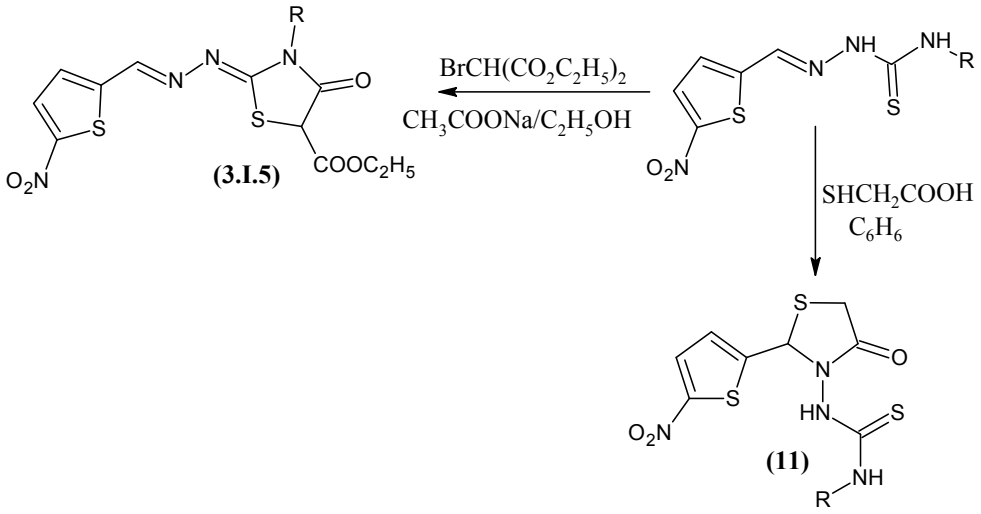
Ethyl 2- bromo propionate or benzyl 2-bromo acetate cyclized with enamino lactones in the presence of absolute ethanol containing 3 equimolars of anhydrous sodium acetate and acetic acid as catalyst, afforded the derivatives of 4- thiazolidinones[6]**(8)**.



Methyl 2-bromo-3-(4-fluorophenyl)propanoate react with $(NH_2)_2CS$ in the presence of NaOAc gave substituted 5-(4-fluorobenzyl)-2-imino-1,3-thiazolidin-4-one [7] **(9)** compounds.



Thiosemicarbazoneswere reacted with various reagents, such as diethyl-2-bromomalonate, thioglycolicacid, and acetic anhydride, to afford heterocyclic substituted thiazolidinonederivatives [8] **(10)** and **(11)**respectively.

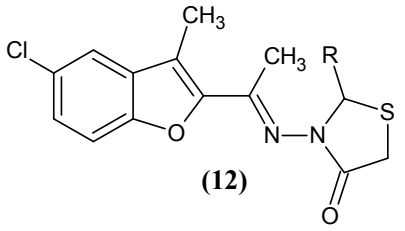


Pharmacological aspects: The chemistry of thiazolidin-4-one ring systems is of considerable interest as it is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities[9]Thiazolidin-4-one derivatives are known to exhibit diverse bioactivities such as antidiarr-

heal [10] anticonvulsant [11] antimicrobial [12] antidiabetic [13] antihistaminic [14] anticancer [15] antiHIV [16] Ca^{2+} channel blocker [17] PAF antagonist [18] cardioprotective [19] anti-ischemic [20] cycloxygenase inhibitory [21] anti-platelet activating factor [22], non-peptide thrombin receptor antagonist [23] and tumor necrosis factor-α antagonist activities [24]. 2-Imino-thiazolidin-4-ones have also been found to have pharmacological activities [25-27]. Many thiazolidine derivatives have been demonstrated to possess antibacterial [28] antifungal [29,30] anticonvulsant [31] anticancer [32] and antituberculosis [33] activities. In addition, thiazolidines have been reported as novel inhibitors of the bacterial enzyme Mur B that was precursor acting during the biosynthesis of peptidoglycan [34]. Furthermore, antibacterial [35], antifungal [36], insulin releasing [37] carbonic anhydrase inhibitory [38], antiinflammtory [39], cardiotonic [40], antimicrobial [41] and antitumor [42] properties of sulfamoyl moiety were described.

Antitubercular activity

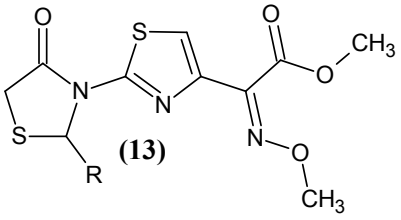
Basawaraj and coworkers synthesized derivatives of 3-{[-1-(5'-Chloro-3'-methyl-1'-benzofuran-2'-yl)ethylidine]amino}-2-substitutedphenyl-1,3-thiazolidin-4-ones [43]**(12)** from 5-Chloro-3-Methyl benzofuran. The synthesized compounds were screened for their antitubercular, antimicrobial and anticonvulsant activities.



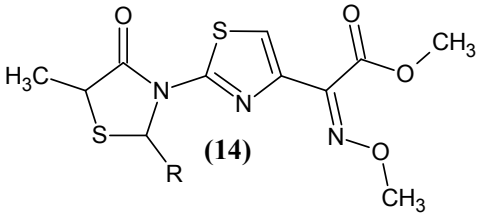
(12)

R= C_6H_5, $C_6H_4(OH)$, C_6H_4Cl

2-Aryl-3-(4'-α-methoxyiminocarbomethoxymethylthiazol-2'-yl)-5-H-4-thiazolidinones **(13)** and 2-aryl-3-(4'-α-methoxyiminocarbmethoxymethylthiazol-2'-yl)-5-methyl-4-thiazolidin-ones **(14)** were synthesized by Parekh and coworkers [44]. All the compounds reported were tested *in vitro* for their antimicrobial and antifungal activityagainst various microorganisms under identicalconditions. Compoundsshowed 80-90% inhibition against *Mycobacteriumtuberculosis H37 RV*.

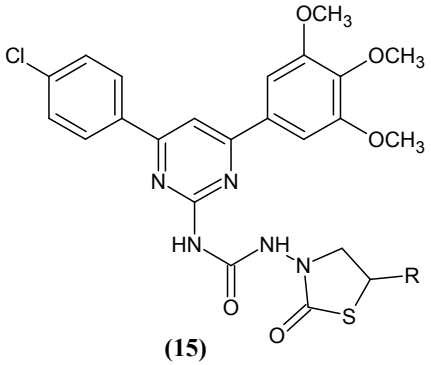


(13)



(14)

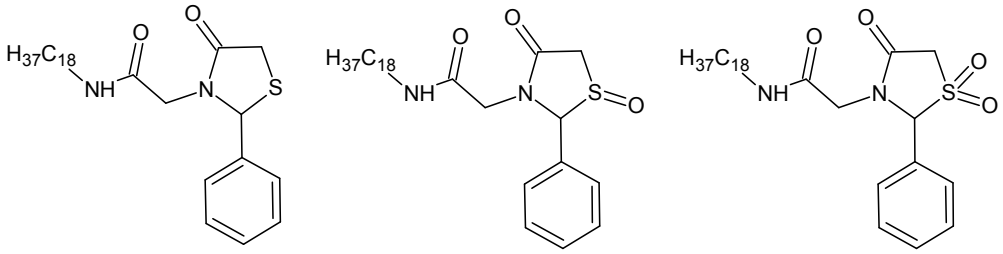
Chikhalia*et al* [45] have synthesized some pyrimidine based thiazolidinones**(15)** compounds and tested for their antimicrobial and antitubercular activity.



(15)

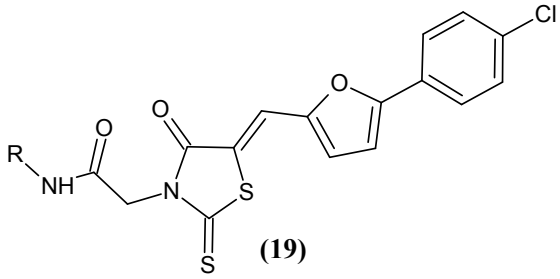
Anticancer activity

Gududuru*et al* [46]described the synthesis and biological evaluation against prostate cancer cells of some 2-aryl-4-oxo-thiazolidin-3-yl amides **(16), (17)** and **(18)**. 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 detected, which are effective in killing prostate cancer cells with improved selectivity compared to serine amide phosphates.



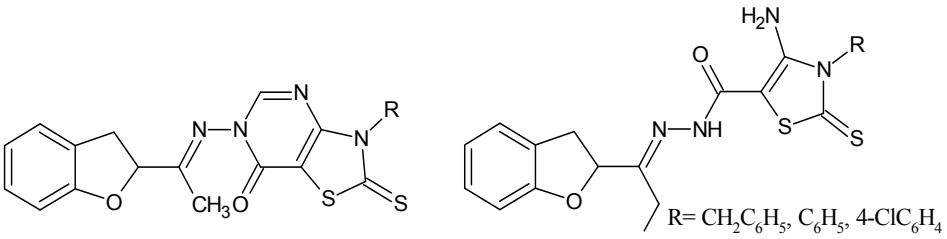
(16) **(17)** **(18)**

A series of 2-(5-((5-(4-chlorophenyl)furan-2-yl)methylene)-4-oxo-2-thioxo thiazolidin-3-yl) acetic acid[47]**(19)** derivatives were synthesized by the coupling of different amines containing aliphatic, substituted aromatic, and heterocyclic moieties. The compounds have shown good antitumor and anti-angiogenic effects against transplantable mouse Ehrlich as cites tumor. Further studies on the thiazolidinone derivatives are of great importance because the compounds may lead to potential therapeutic agents for treatment of cancer.



(19)

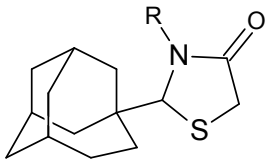
Samianes and co workers[48] have synthesized 2-thioxo-2,3-dihydro-thiazoles **(20)** and 2-thioxo-2,3-dihydro-6H-thiazolo[4,5-d]pyrimidin-7-ones **(21)**. The compounds were evaluated for their *in vitro* anti-HIV, anticancer, antibacterial, and antifungal activities. Some compounds, showed weak activity against breast and lung cancer. Thiazolidinone amides, carboxylic acids, serine amides were synthesized and tested for possible anticancer activity[49-54].



(20) **(21)**

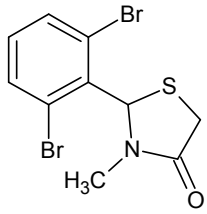
Anti HIV

2-Adamantyl-substitutedthiazolidin-4-ones **(22)** were synthesized by Balzarini*et al*[55] and evaluated for activity against HIV-1 (IIIB) and HIV-2(ROD) in CEM cell cultures, by taking *Nevirapine* as reference compounds.



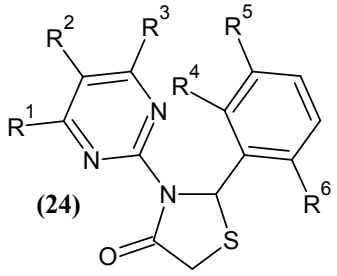
(22)

Rawal hasreported 2-(2,6-dibromophenyl)-3-heteroaryl-1,3-thiazolidin-4-one **(23)** derivatives. A positive correlation between size of the halogen substituent and HIV-RT inhibitory activity was taken as for the synthesis[56].



(23)

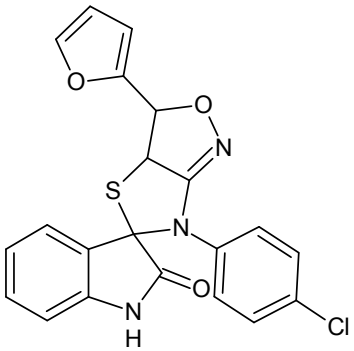
A series of 1,3-thiazolidin-4-ones **(24)** were synthesized by Ravichandran and his co-workers[57] and evaluated against anti HIV activity.



(24)

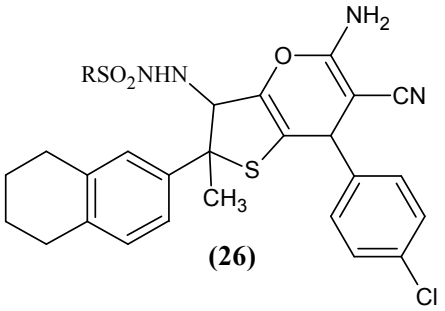
Anti analgesic activity

Nilanjan*et al*[58] have synthesized many derivatives of 3-(p-chlorophenyl)6-Furyl-cis-5a,6-dihydro spiro[3H-indole3,4-thiazolo(5,1-c)isoxazolo-2(1H)-one] **(25)**. Compound were evaluated for analgesic activity by tail flick method and the results shows that synthesized compound possess significant analgesic activity when compared with *nimuslide* as standard.



(25)

Omar *et al*[59] synthesized some tetrahydronaphthalen-2-yl heterocycle **(26)** and **(27)**compounds. All the compounds were tested for analgesic as well as antiinflammatory activity.The carrageenan rat paw edema model of inflammation was used to evaluate the anti-inflammatory properties of the tested compounds



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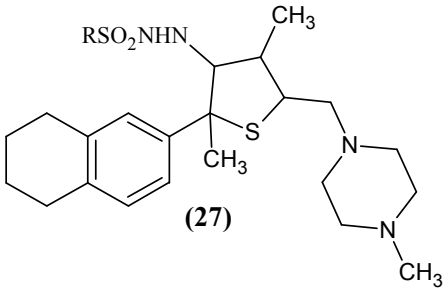

(27)

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