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Review Article

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Thiazolidinone as a pharmacologically active molecule

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ABSTRACT

Thiazolidinones, among the various heterocyclic compounds has drawn attention because of its various pharmacologically activities associated with it. A lot of research work has been done on synthetic schemes and biological activities of various thiazolidinone derivatives over the years. This review article focuses on the pharmacological profile of thiazolidinone and its derivatives with examples in form of figures.

Keywords: Thiazolidinone, Pharmacological activity, Anti-inflammatory, Antimicrobial, Anticancer

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INTRODUCTION

Heterocyclic compounds are the essential part of chemical and life sciences. Thiazolidinone belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five member ring. Thiazolidinones are saturated form of thiazole, that have an atom of sulfur at position 1, an atom of nitrogen at position 3 and a carbonyl group at position 2, 4, or 5. Substituents in the 2-, 3-, and 5-positions may be varied, but the greatest difference in structure and properties is exerted by the group attached to the carbon atom in the 2-position. 4-Thiazolidinones are derivatives of thiazolidine with a carbonyl group in the 4-position. The carbonyl group of thiazolidinone is highly unreactive while when 4-thiazolidinone reacted with Lawesson's reagent gives corresponding 4-thione derivatives.

There are various biologically active heterocyclic compounds which contain various heteroatoms such as nitrogen, sulphur and oxygen. 4-Thiazolidinone is an important moiety as it has almost all types of biological activities which has encouraged interest for further synthesizing several new compounds containing various heterocyclic rings, attached to 4-thiazolidinone moieties. The diverse biological activities include anti-inflammatory, analgesic, antimicrobial, anti-proliferative, antiviral, anticonvulsant, anti-diabetic, antihyperlipidemic, cardiovascular, anti-tubercular, antifungal, antibacterial and antitumor activity on leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate and breast cancers cell lines.

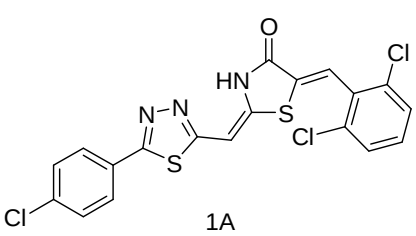
Thiazolidinones go through different types of reactions to give other heterocyclic compounds. Eg. Thiazole, benzimidazole, thiopyrano- thiazolone, benzodiazepine, triazoles, benzothiophenes.

BIOLOGICAL ACTIVITIES OF THIAZOLIDINONE DERIVATIVES

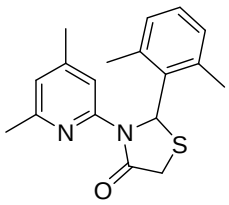
ANTIVIRAL

A novel series of 5-arylidene-4-thiazolidinones were synthesized by I. Küçükgüzel *et al.* and were evaluated as HCV NS5B polymerase inhibitors. Compound 1A was found to be most active antiviral agent [1].

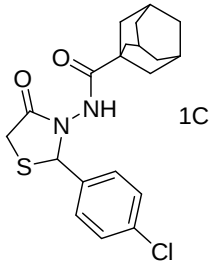
A new series of 1,3-thiazolidin-4-one derivatives were prepared, characterized and evaluated for their in vitro antibacterial, antifungal, and anti-viral activities by Ravichandran *et al*. Structure–activity relationship studies revealed that the nature of the substituents at the 2 and 3 positions of the thiazolidinone nucleus had a significant impact on the in vitro antimicrobial and anti-viral activity of these classes of agents. Compound **1B** was found to have good antiviral activity against Influenza A H3N2 subtype and Influenza B [2].



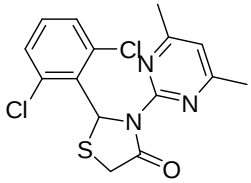
1A



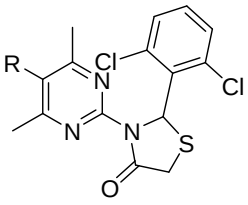
1B



1C

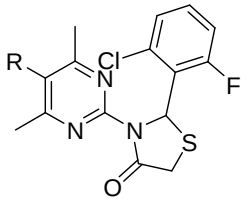


1D

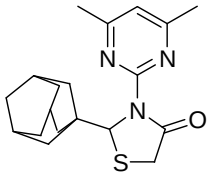


E(a-i)

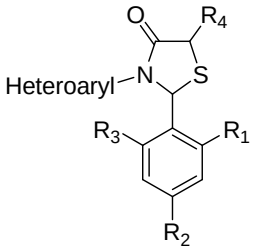
R	
a	H
b	CH3
c	CH2CH3
d	CH2CH2CH3
e	CH2(CH2)2CH3
f	CH2(CH2)3CH3
g	CH2CH=CH2
h	CH2CH2C=N
i	Br



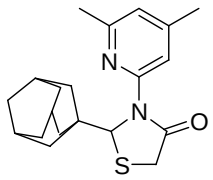
F(a-i)



1G



Cpd.	Heteroaryl	R_1	R_2	R_3	R_4
1H	Pyridin-2-yl	H	F	H	H
1I	Pyridin-3-ylmethyl	Cl	H	Cl	CH_3
1J	Furan-2-ylmethyl	Cl	H	Cl	CH_3



1G

G.S. Hassan *et al.* designed and synthesized a new series of 1-adamantyl thiazolidinone derivatives. From which some were evaluated for antiviral activity against Herpes simplex type1 (HSV-1) grown on Vero African green monkey kidney cells. The results showed that some compounds showed antiviral activity and derivative **1C** was most active [3].

V. Murugesan *et al.* performed comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA) based 3D QSAR study of 2,3-diaryl-1,3-thiazolidin-4-one derivatives as HIV-1 reverse transcriptase (HIV-1 RT) inhibitors using global minima and crystal structure conformations for understanding the structural requirements of these inhibitors which provided predictive and diagnostic value for the modification of thiazolidin-4-one analogues. The most active compound was found to be **1D** [4].

A novel series of thiazolidin-4-ones which has a hydrophobic substituent at 5-position on the 4,6-dimethylpyrimidine ring at N-3 **[1E(a-i)&1F(a-i)]** were designed for QSAR studies and synthesized by H. Chen *et*

al. which were then evaluated as HIV-1 reverse transcriptases inhibitors and showed that some of the new compounds effectively inhibit RT activity [5].

A series of novel thiazolidin-4-ones having a lipophilic adamantyl substituent at position 2 or 3 were synthesized by J. Balzarini *et al.* and were evaluated for their inhibitory activity against HIV-1(IIIB) and HIV-2(ROD)-induced cytopathicity in CEM cell cultures. **Compound 1G** showed good anti-HIV activity [6].

V. Ravichandran *et al.* performed 3D-QSAR study of 96 molecules to explore the structural requirements of thiazolidinone derivatives which indicated that 2', 3", 6" substituted aromatic rings of thiazolidinones are important for anti-HIV activity, which can efficiently guide further modification of thiazolidinone analogs [7].

A novel series of 2,3-diaryl-1,3-thiazolidin-4-one derivatives were synthesized by Rawal *et al.* and were evaluated for their ability to inhibit HCV NS5B. **1H, 1I and 1J** were more potent, displaying over 95% inhibition of NS5B RNA polymerase activity *in vitro* [8].

J. Balzarini *et al.* 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, several compounds exhibited a potent anti-HIV-1 activity. **Compound 1K** was found to be most active [9].

ANTIDIABETIC

A series of 5-(carbamoylmethoxy)benzylidene-2-oxo/thioxo-4-thiazolidinone derivatives were synthesized by R. Maccari *et al.* as inhibitors of aldose reductase (AR), enzyme which plays a crucial role in the development of diabetes complications as well as in the inflammatory processes associated both to diabetes mellitus and to other pathologies**. Compound 2A** was found to be most active [10].

A new series of 2-hydrazolyl-4-thiazolidinone-5-carboxylic acids with pyrazolyl pharmacophore was synthesized by M. R. Bhosle *et al.* and evaluated for the antihyperglycemic activity in sucrose loaded rat model and among those compounds **2B**, **2C** and **2D** displayed good antihyperglycemic activity [11].

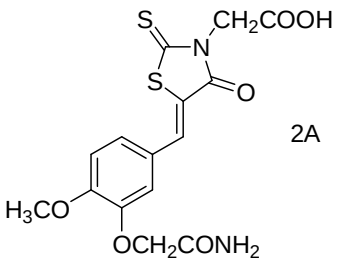
A series of thiazolidinone derivatives **(2E)** was synthesized and evaluated for their hypoglycemic activity using alloxan-treated female albino mice by Faidallah, H. *et al* [12].

Kini and Ghate studied the oral hypoglycaemic activity of some new thiazolidinone derivatives (2F) and found that electro-negativity is responsible for variation in hypoglycemic activity [13].

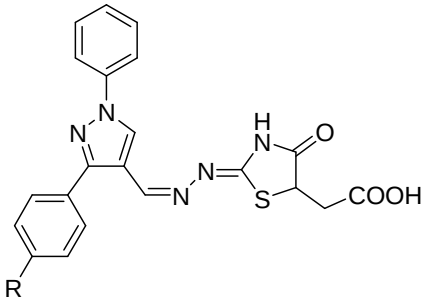
A new series of 5-arylidene-2-thioxo-4-thiazolidinone derivatives **(2G)** were prepared by Maccari, R. *et al.* and most of the compounds were found to be moderate in aldose reductase inhibitory effects at low micromolar doses [14].

Liu *et al.* studied a series of thiazolidinone-substituted biphenyl scaffold as PTP1B inhibitors and reported that introduction of the 4-oxothiazolidine-2-thione moiety showed better inhibitory activity against PTP1B. Compound **2H** showed good results [15].

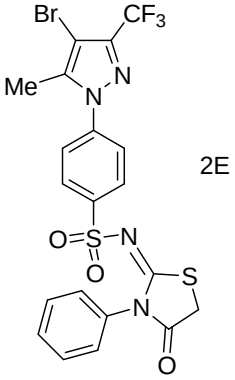
Ottana, A *et al*. synthesized a novel thiazolidinone series and found that unsubstituted derivative **(2I)** at para position of the distal phenyl ring proved to be most active in this series as antidiabetic agent [16].



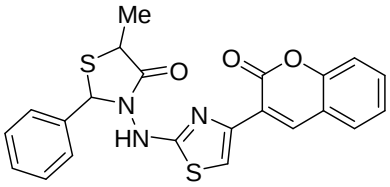
2A



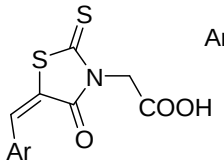
	R
2B	-F
2C	-NO2
2D	-OH



2E

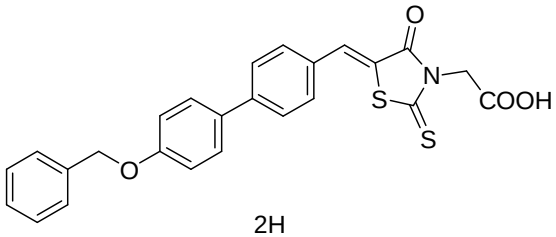


2F

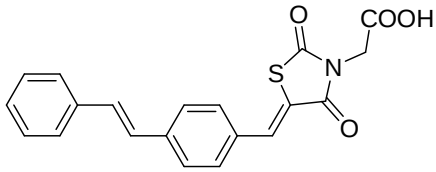


Ar= 3-O-C_6H_5-C_6H_5
4-OC_6H_5-C_6H_5
3-OCH_2-C_6H_5-C_6H_4
4-OCH_2-C_6H_5-C_6H_4
3-OCH_3-C_6H_4

2G



2H



2I

ANTICANCER

K. S. Sharath Kumar *et al*. studied 2,3 disubstituted 4-thiazolidinone derivatives for antiproliferative and tumor inhibitory activity and found that compound **3A** was most active [17].

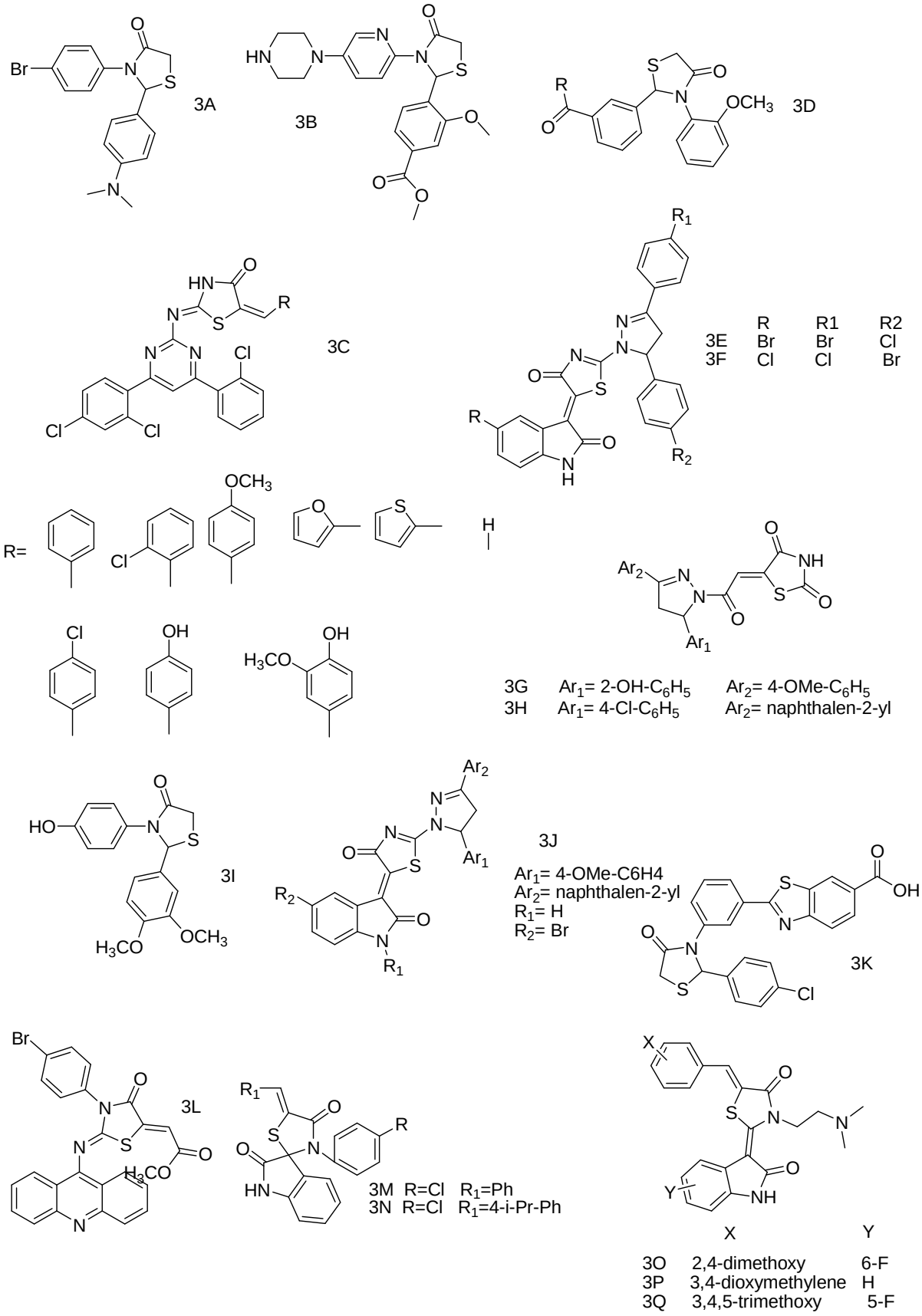
A new series of 2,3 disubstituted 4-thiazolidinone analogues was synthesized by K. S. Sharath Kumar *et al.* and antiproliferative effect on human leukemic cells was evaluated. Compound **3B** displayed potent activity against Nalm6, K562, Jurkat cells [18].

Mohd Rashid *et al.* designed and synthesized some new pyrimidine clubbed thiazolidin-4-one derivatives (**3C)** and their in vitro anticancer activities were screened at National Cancer Institute (NCI), USA against full NCI 60 cell lines which showed good to remarkable anticancer activity [19].

A new series of 2,3-diaryl-4-thiazolidinone analogs was synthesized by J. Wu *et al.* and evaluated for their antiproliferative properties against tumor cell proliferation and migration. *In vivo* study indicated that compound **3D** suppresses tumor growth and metastasis as well as promote survival rate [20].

S. Avdieiev *et al.* screened new thiazolidinone derivatives and found that this is a novel group with promising anti-tumour compounds which inhibited proliferation of MCL cells **3E** and **3F** were found to be most active [21].

D. Havrylyuk *et al.* synthesized a series of novel 5-pyrazoline substituted 4-thiazolidinones and evaluated for their anticancer activity in vitro. Among them **3G and 3H** were found to be the most active [22].



M. Sala *et al.* synthesized 2,3-thiazolidin-4-one derivatives from resveratrol (RSV) and evaluated for cytotoxic activity of on human breast cancer cell lines. The result indicated that some of thiazolidin-based resveratrol

derivatives may become a new potent alternative tool for the treatment of human breast cancer. The most active compound was **3I** [23].

Dmytro Havrylyuk *et al.* synthesized some novel 4-thiazolidinone derivatives and were screened for their *in vitro* antitumor activity by the National Cancer Institute. The most effective anticancer compound **3J** was found to be active emphasizing the importance of the presence and positioning of a central linker (4-thiazolidinone moiety) between two terminal heterocycles (indolone and pyrazoline) [24].

A new series of thiazolidinone substituted benzothiazole-6-carboxylic derivatives was prepared by P. P. Prabhu *et al.* and were screened for their *in vitro* anticancer activity by MTT assay on human cervical cancer cell line (HeLa) cell lines. Compound **3K** exhibited most significant activity [25].

H. Paulíková *et al.* synthesized three new acridine–thiazolidinone derivatives and studied their interactions with calf thymus DNA and a number of cell lines (leukemic cells HL-60 and L1210 and human epithelial ovarian cancer cell lines A2780), **3L** was found to have highest activity in cytotoxic tests [26].

D. Kaminskyy *et al.* synthesized a new series of spiro[thiazolidinone-isatin] congugates and were screened *in vitro* for anticancer activity in the National Cancer Institute. Compound **3M** and **3N** were found to be more active [27].

A series of novel 4-thiazolidinone was designed and synthesized by S. Wang *et al.* and **3O, 3P, 3Q** were evaluated for cytotoxic activities *in vitro* against three human cancer cell lines including HT-29 (human colon cancer), H460 (human lung cancer), MDA-MB-231 (human breast cancer) by MTT assay [28].

ANTIINFLAMMATORY

Two series of new thiazolidin-4-one derivatives were designed and synthesized by K.R.A. Abdellatif *et al.* which were evaluated for their in vitro COX-2 selectivity and anti-inflammatory activity in vivo. Compounds **4A** and **4B** showed the best overall in vitro COX-2 selectivity and in vivo activities [29].

R. Maccari *et al.* synthesized a series of 5-(carbamoylmethoxy)benzylidene-2-oxo/thioxo-4-thiazolidinone derivatives as inhibitors of aldose reductase (AR), enzyme which plays a crucial role in the development of diabetes complications as well as in the inflammatory processes associated both to diabetes mellitus and to other pathologies. Compound **4C** proved to be most active compound [30].

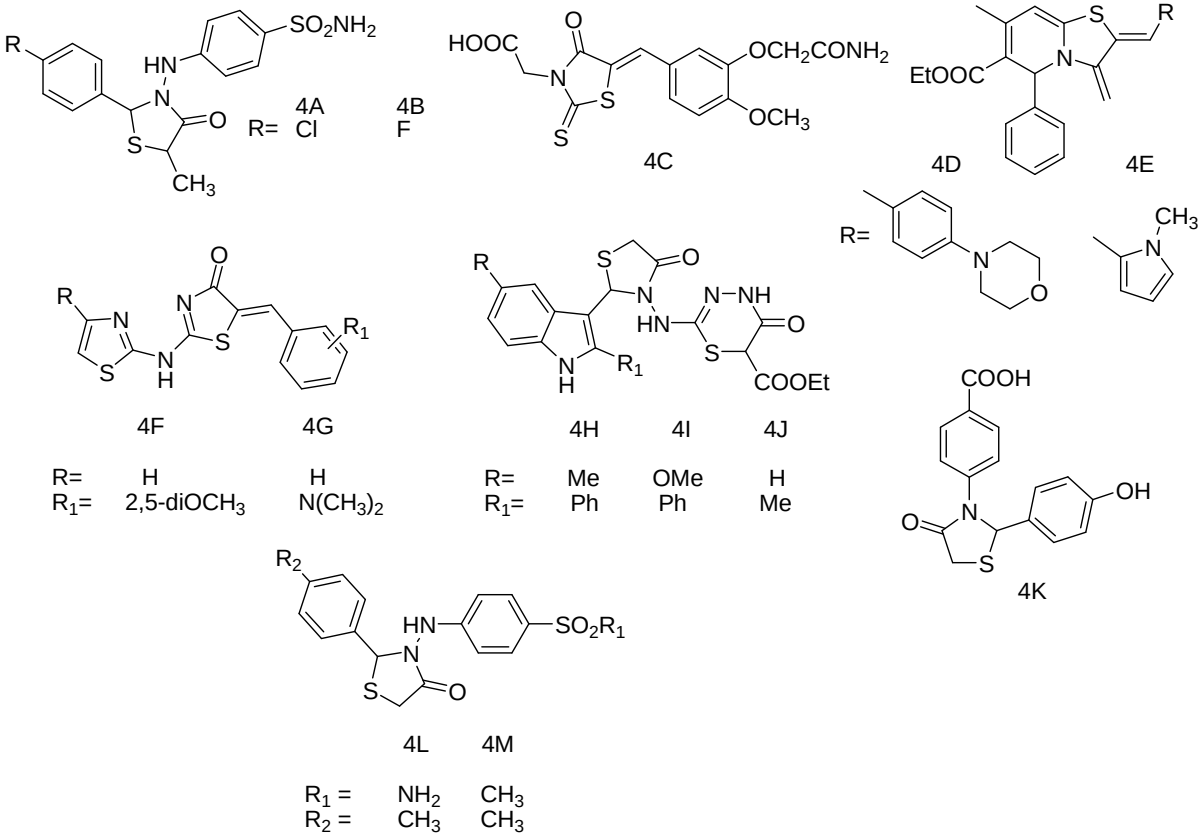
J. Hu *et al.* synthesized and biologically evaluated four new series of novel thiazolidinone derivatives and screened for anti-inflammatory activities. Compounds **4D** and **4E** inhibited LPS-induced TNF-α and IL-6 release in a dose-dependent manner [31].

Novel 5-arylidene-2-(1,3-thiazol- 2-ylimino)-1,3-thiazolidin-4-ones were synthesized and biologically evaluated for dual anti-inflammatory/antimicrobial activity by I. Apostolidis *et al.* Compound **4F** is the most potent LOX inhibitor, whereas compound **4G** presents the highest anti-inflammatory activity and 50% COX-1 inhibition [32].

A novel Indolyl 4-thiazolidinones bearing thiadiazine nucleus was synthesized **by D.P. Anekal and J.S. Biradar** and then selected compounds were evaluated for analgesic and anti-inflammatory activities. Compounds **4H, 4I** and **4J** found to have significant activity [33].

A series of 4- thiazolidinone derivatives were synthesized from 4-amino benzoic acid by M. Sugumaran *et al.* The two synthesized compounds were screened for anti-inflammatory and analgesic activity. Compound **4K**, showed better activity due to the presence of electron donating group such as hydroxy group at the 2nd position of 4-thiazolidinone [34].

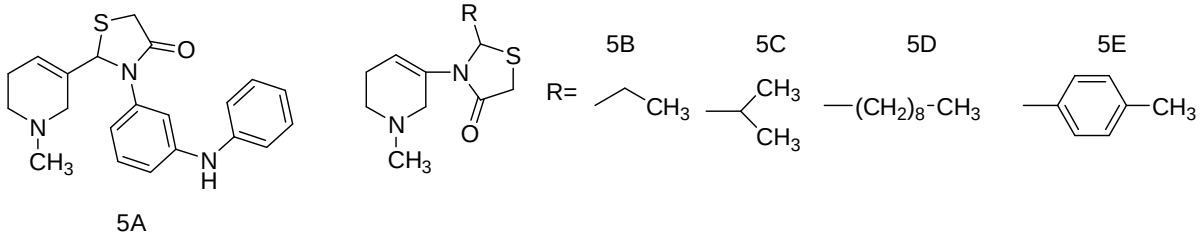
O. Unsal-Tan *et al.* designed a series of novel 2-aryl-3-(4-sulfamoyl/ methylsulfonylphenylamino)-4-thiazolidinones as new selective cyclooxygenase-2 inhibitors. The designed compounds with reasonable binding modes and high docking scores were synthesized. Compounds **4L** and **4M** which have methyl group on the phenyl ring were most potent [35].



ANTIALZHEIMER

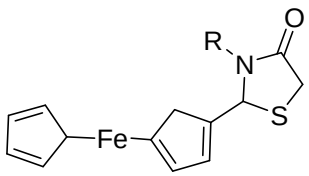
A new series of novel N-alkyl/aryl substituted thiazolidinone arecoline analogues designed and synthesized by **C.T.** Sadashiva *et al.* and screened for muscarinic receptor 1 agonist in Alzheimer's dementia models. Compound **5A** which contains diphenylamine moiety attached to N of thiazolidinone was found to have maximum activity [36].

J.N.N.S. Chandra *et al.* synthesized a series of arecoline thiazolidinones which were evaluated for *in vitro* muscarinic receptor binding studies and *in vivo* pharmacological evaluation of memory and learning in male Wistar rats. Four derivatives **5B, 5C, 5D** and **5E** showed significant activity [37].



ANTI-ANXIETY

Pejović A. *et al.* prepared a small library of *N*-substituted 2-ferrocenyl-1,3-thiazolidin-4-ones **6(A-M)** and evaluated for anxiolytic properties in different *in vivo* models as novel $GABA_A$ benzodiazepine-binding site ligands. Study showed that incorporation of the ferrocene core and fine tuning of the distance between the thiazolidinone core and an additional aromatic ring were crucial structural requirements for the observed anxiolytic effect [38].



6(A-M)

R

A n-butyl
B n-pentyl
C n-hexyl
D n-octyl
E n-dodecyl
F n-hexadecyl
G 2-(p-methoxyphenyl)ethyl
H benzyl
I 2-furfuryl
J 2-thienyl
K phenyl
L m-tolyl
M p-tolyl

ANTIPSYCHOTIC AND ANTI-CONVULSANT

Velmurugan. V *et al.* synthesized and investigated the anticonvulsant activity of thiazolidinone derivatives using maximal electroshock-induced seizure (MES) in mice which showed better activity. Compound **7A** was found to be most active [39].

J. Dwivedi *et al.* synthesized a series of thiazolidinone derivatives and evaluated for antiepileptic activities using maximum electro seizure method. Compound **7B** having good lipophilicity was found to be most active [40].

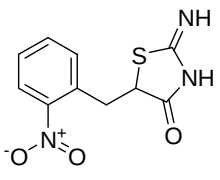
Kaur *et al.* synthesized novel substituted thiadiazolylazetidinonyl and screened for their anticonvulsant activities. It was concluded that among the various derivatives **7C** showed promising anti-convulsant activity [41].

Shingalapur *et al.* prepared a series of 4-thiazolidinones containing 2-mercapto benzimidazole moiety and were screened for in-vivo anticonvulsant activity by Maximal Electroshock (MES) model. The compounds **7D, 7E, 7F** and **7G** exhibited potent anticonvulsant activity [42].

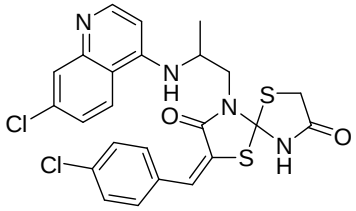
Mahendra R. Shiradkar *et al.* synthesized two new series of clubbed thiazolidinone–barbituric acid and thiazolidinone–triazole derivatives which were then evaluated for their anticonvulsant activity in two animal models of seizures, *viz.* maximal electroshock seizure (MES) and subcutaneous pentylenetetrazole (scPTZ) and found with no or less neurotoxicity. They exhibited excellent anticonvulsant activity in both animal models of seizure. Compounds **7H, 7I, 7J** and **7K** exhibited maximum activity [43].

A series of 5-[(2′-substituted phenyl-4′-oxothiazolidin-3′-yl)amino]-2-oxo/thiobarbituric acids was synthesized by A. Agarwal *et al.* which was subjected for in vivo studies for anticonvulsant and acute toxicity studies. Compounds **7L** and **7M** were most potent compounds [44].

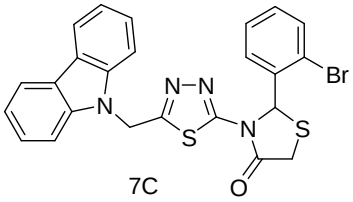
Aysel Gursoy *et al.* synthesized two regioisomer series. From the series two compounds were selected and subjected to anticonvulsant activity tests using the maximal electroshock seizure (MES) and subcutaneous pentetrazol seizure (ScMet) tests.Compound **7N** showed promisingly active [45].



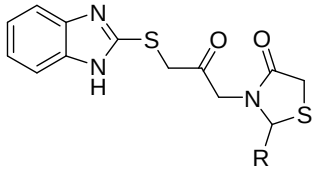
7A



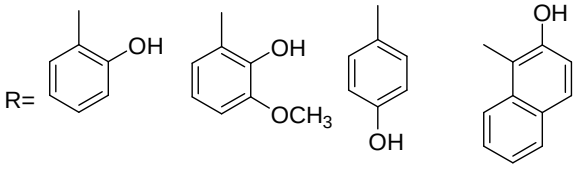
7B

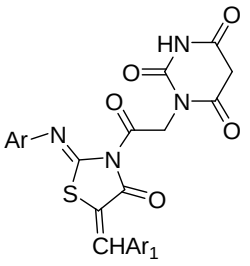


7C



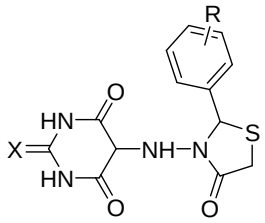
7D 7E 7F 7G





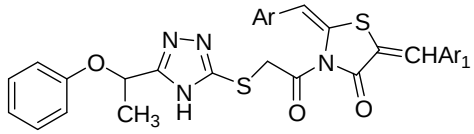
7H 7I

Ar= -2-OHC$_6$H$_4$ -2-OHC$_6$H$_4$
Ar$_1$= -2-OHC$_6$H$_4$ -4-CH$_3$C$_6$H$_4$



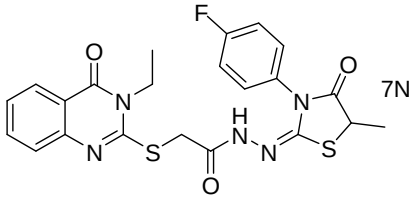
7L 7M

X= S S
R= m-OCH$_3$,p-OH p-N(CH$_3$)$_2$



7J 7K

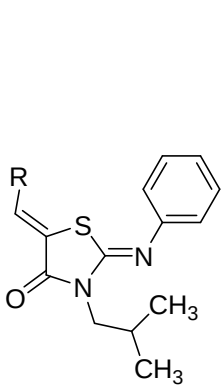
Ar= -2-OHC$_6$H$_4$ -2-OHC$_6$H$_4$
Ar$_1$= -2-OHC$_6$H$_4$ -4-CH$_3$C$_6$H$_4$

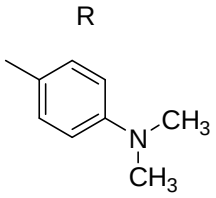


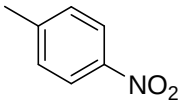
7N

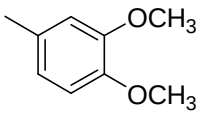
ANTIAMOEBIC

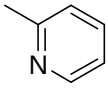
Md. Mushtaque *et al.* synthesized a series of thiazolidinone derivatives were synthesized screened *in vitro* against HM1:IMSS strain of *E. histolytica*. Some of the compounds showed better antiamoebic activity than reference drug metronidazole with low cytoxicity. Compounds **8A, 8B, 8C** and **8D** showed good activity with low toxicity [46].



8A 

8B 

8C 

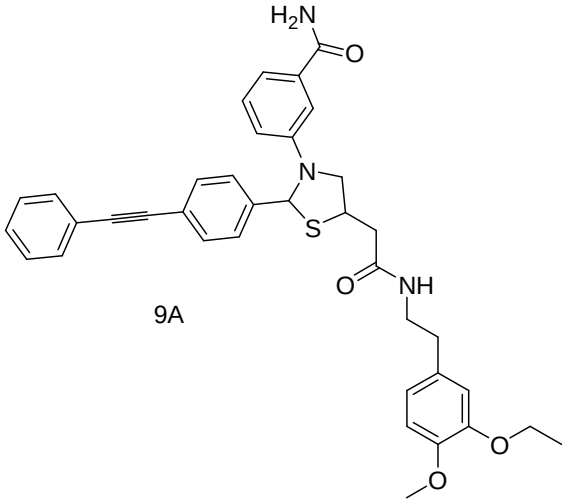
8D 

FSH RECEPTOR AGONIST

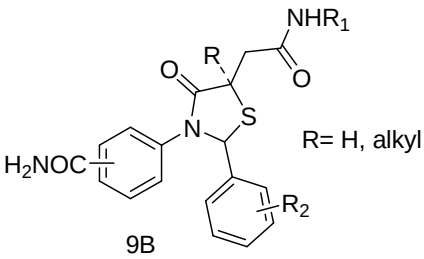
V. Sriraman *et al.* investigated in detail the ability of thiazolidinone derivative **9A** to activate FSH signalling and learn the barriers that preclude development of this derivative for clinical purposes. The results showed that it was FSHR allosteric modulator but with poor oral FSH receptor modulator [47].

A potent analog **9B** of thiazolidinone-based follicle-stimulating hormone (FSH) agonists, which contains an additional 5-alkyl substituent, was prepared and evaluated in a Chinese hamster ovary (CHO) cell line that expressed recombinant human FSH receptor (FSHR) and a luciferase reporter gene regulated by a cAMP response element (CRE) by Arey *et al*. The derivatives also showed good potency in the CRE-luciferase assay [48].

Jetter *et al.* evaluated few 5-alkylated thiazolidinones derivatives as FSH receptor agonist and the replacement of the 5-hydrogen **(9C)** with a 5-methyl moiety **(9D)** lead to increased agonist activity while replacement with allyl moiety displayed full agonist efficacy [49].

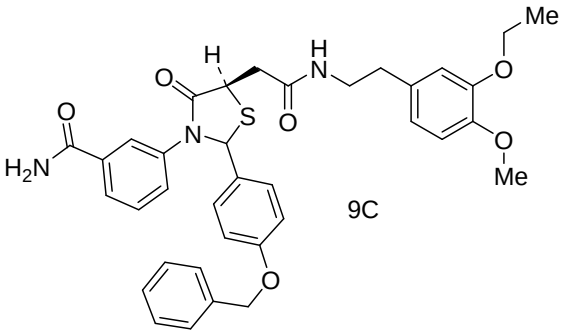


9A

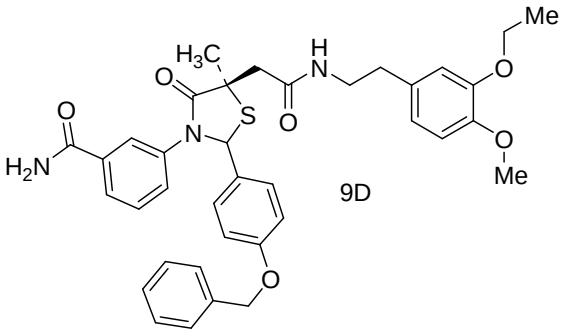


9B

R= H, alkyl



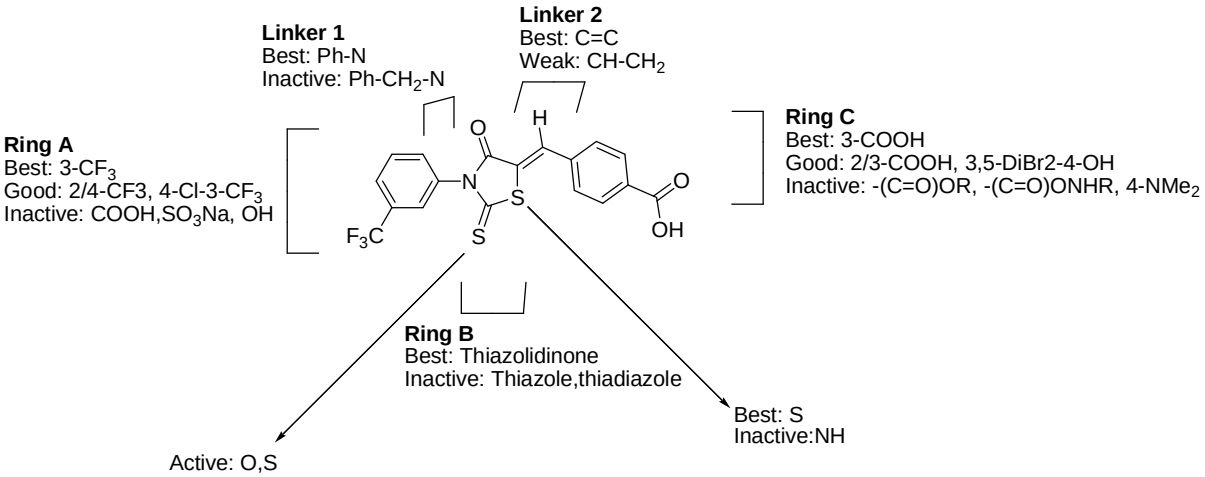
9C



9D

CYSTIC FIBROSIS

Sonawane *et al.* synthesized a series of 3-[(3-trifluoromethyl) phenyl]-5-[(3-carboxyphenyl)methylene]-2-thioxo-4-thiazolidinone **(10A)**.Greatest CFTR inhibition potency was found for 3-CF3 and polar group-substituted-phenyl rings, and a thiazolidinone core [50].

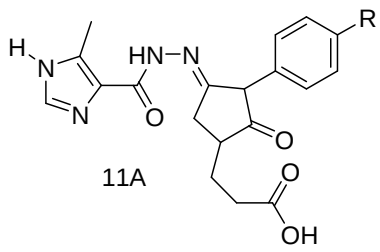


ANTITOXOPLASMA GONDII

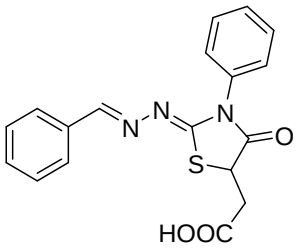
Liesen *et al*. synthesized three new series of compounds from ethyl (5-methyl-1-H-imidazole-4- carboxylate): acylthio-semicarbazide analogs, 4-thiazolidinone analogs **(11A)** and 1,3,4-thiadiazole analogs. The majority of the tested compounds showed excellent anti- *T. gondii* activity [51].

De Aquino *et al.* synthesized a new series of 2-[(phenylmethylene) hydrazono]-4-oxo-3-phenyl-5-thiazolidineacetic acids **(11B)**. The *in vitro* anti-*T. gondii* activity of synthesized compounds was evaluated and they promoted decrease in the percentage of infected cells leading to parasite elimination [52].

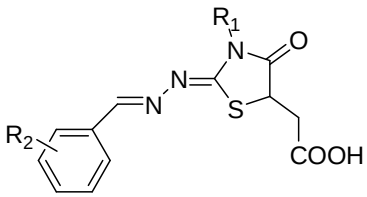
Synthesis and evaluation of anti *T. gondii* activity of 4-thiazolidinones derivatives **(11C)** substituted at arylhydrazone moiety with electron-withdrawing or electron-donating groups, and at N- 3 position with H, methyl, ethyl and phenyl substituents has been reported by R. P. Tenorio *et al* [53].



11A



11B



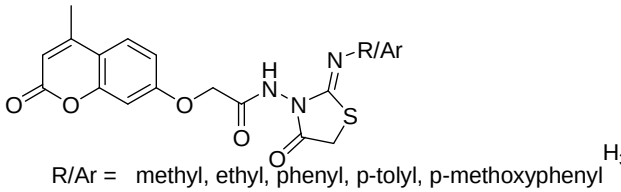
11C

ANTIOXIDANT

B. Šarkanj *et al.* synthesized a series of thiazolidinone derivatives **12A** and investigated their antioxidant, metal-chelating and antifungal activities which were compared to the activity of the starting material, 7-hydroxy-4-methylcoumarin, and were proven to possess potent antioxidant and antifungal activity [54].

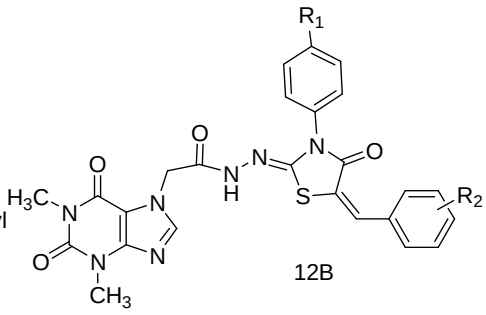
Florentina Geanina Lupascu *et al.* synthesized new benzylidenethiazolidin-4-one derivatives and *in vitro* antioxidant potential was evaluated according to the ferric reducing power, the total antioxidant activity and the DPPH and ABTS radical scavenging assays. All derivatives were found to be more active than their parent thiazolidin-4-ones [55].

A series of sydnonyl substituted thiazolidinone derivatives were synthesized by M.-H. Shih and F.-Y. Ke and evaluated for their antioxidant activity. The antioxidant activity of derivatives **12C** have been found to exhibit the significant DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activity, comparable to that of vitamin E [56].



R/Ar = methyl, ethyl, phenyl, p-tolyl, p-methoxyphenyl

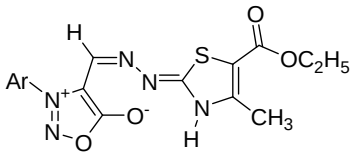
12A

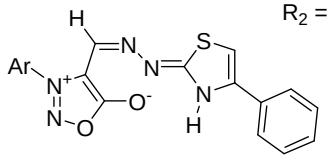


12B

R_1 = H, Cl

R_2 = H, F(4), Cl(4), Br(4), OH(4), $N(CH_3)_2$(4), NO_2(2)





12C

Ar= C_6H_5, p-$CH_3C_6H_4$, p-CH_3-OC_6H_4, p-C_2H_5-OC_6H_4

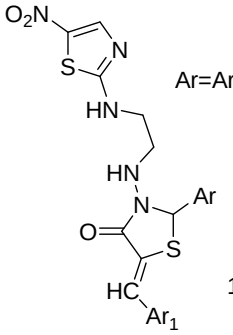
ANTITUBERCULAR

P. Samadhiya *et al*. synthesized a new series of N-[2-{2-(substitutedphenyl)-4-oxo-5-(substitutedbenzylidene)-1,3-thiazolidine}-iminoethyl]-2-amino-5-nitrothiazole derivatives **13A**, which were screened for antitubercular activity by screening against *Mycobacterium tuberculosis*. All the derivatives showed good activity [57].

A series of compounds 4-oxo-thiazolidine derivatives **13B** were synthesized by D.R. Godhani *et al.* and were screened *in vitro* for antitubercular activity against *Mycobacterium tuberculosis* H37Rv and all were found to be moderately active [58].

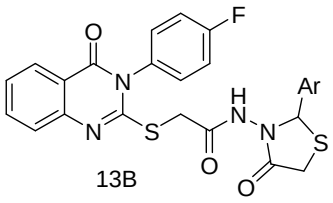
Narute *et al.* did QSAR study on a series of (substituted 1, 2-dihydro) 4-thiazolidinones bearing benzothiophene nucleus **13C**, for antitubercular activity which was carried out by taking into consideration various physicochemical descriptors. Two models were selected which highlight some common important features i.e. bulky substitution and high neucleophilic nature of compounds that increase antitubercular activity [59].

Pyrimidine based thiozolidinones (**13D)** were synthesized by K. H. Chikhalia *et al.* and were tested for antitubercular activity against *M. Tuberculosis* [60].

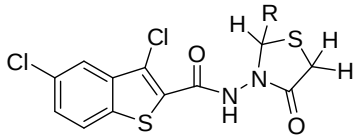


13A

Ar=Ar_1=substituted phenyl ring=C_6H_4, $4ClC_6H_4$, $3ClC_6H_4$, $2ClC_6H_4$, $4BrC_6H_4$, $3BrC_6H_4$, $2BrC_6H_4$,$4NO_2C_6H_4$, $3NO_2C_6H_4$, $2NO_2C_6H_4$, $4CH_3OC_6H_4$, $4CH_3C_6H_4$, $4HOC_6H_4$



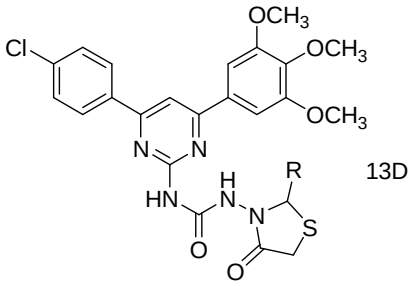
13B



13C

R=3-Br-C_6H_4, 3-Cl-C_6H_4, 3,4-$(OCH_3)_2$-C_6H_3,4-OCH_3-C_6H_4, 3-OCH_3-4OH-C_6H_3,4N,N-$(CH_3)_2$-C_6H_4, 3-OC_6H_5-C_6H_4, 4-S-CH_3-C_6H_4, 3,4,5-$(OCH_3)_3$-C_6H_2

Ar=$4ClC_6H_4$, $3ClC_6H_4$, $2ClC_6H_4$, $4NO_2C_6H_4$, $3NO_2C_6H_4$, $2NO_2C_6H_4$, $4CH_3OC_6H_4$, $3HOC_6H_4$, $2HOC_6H_4$,$4FC_6H_4$



13D

R=3-$NH_2C_6H_4$, 4-$N(CH_3)_2C_6H_4$, 2-$NO_2C_6H_4$, 2-ClC_6H_4, 2,4-$(Cl)_2C_6H_3$,4-FC_6H_4, 2-$OCH_3C_6H_4$, 4-$OCH_3C_6H_4$, 3,4,5-$(OCH_3)_3C_6H_2$, 2-OHC_6H_4`

ANTIMICROBIAL ACTIVITY

N.C. Desai and Amit M. Dodiya synthesized a series of 2-(2-chloro-6-methyl(3-quinolyl))-3-[2-(4-chlorophenyl)-4-oxo(3-hydroquinazolin-3-yl)]-5 [(aryl)methylene]-1,3-thiazolidin-4-ones **(14A)**. In vitro antimicrobial activity of the compounds were screened against some bacteria and fungi. Some derivatives bearing chloro or hydroxyl group exhibited very good antimicrobial activity [61].

Some novel derivatives of 4-thiazolidinone were prepared and evaluated for their in vitro antimicrobial activity against some strains of bacteria and fungi by A. Deep *et al.* All the synthesized compounds showed significant biological activity against the tested microorganisms. **14B** and **14C** were found to be most effective compounds [62].

P. Samadhiya *et al.* synthesized a new series of N-[2-{2-(substitutedphenyl)-4-oxo-5-(substitutedbenzylidene)-1,3-thiazolidine}-iminoethyl]-2-amino-5-nitrothiazole **(14D)**.All the synthesized compounds were screened for their antibacterial and antifungal activities against some selected bacteria and fungi [57].

Synthesis of new series of 3-(4-chloro-2-hydroxyphenyl)-2-(substituted) thiazolidin-4-one was carried out by D.N. Pansare *et al.* and were screened for antimicrobial activity. Among the synthesized compounds **14E, 14F, 14G, 14H** were found to be a broad spectrum molecule active against all bacterial and fungus strains tested [63].

Novel 5-arylidene-2-(1,3-thiazol- 2-ylimino)-1,3-thiazolidin-4-ones were synthesized and biologically evaluated for their antimicrobial and antifungal activities against a panel of Gram positive, Gram negative bacteria and moulds by

I. Apostolidis *et al.* All tested compounds exhibited better antimicrobial activity than commercial drugs, bifonazole, ketoconazole, ampicillin and streptomycin. **14I** was found to be most active as antibacterial agent [32].

J. Dwivedi *et al.* synthesized a series of thiazolidinone derivatives and evaluated for antibacterial activity against two pathogenic strains (*E. coli* and B. *subtilis*) and the antifungal activity was evaluated against two pathogenic strains (*A. niger* and *A. flavus*).Compound **14J** having good lipophilicity is found to be most active against all bacteria and fungi except *B. subtilus* for which compound **14L** showed highest activity and *A. flavus* for which **14K** showed good activity [42].

A novel series of thiazolidinone derivatives was synthesized by D. Patel *et al.* and then evaluated for their antimicrobial activity against eight bacterial strains (*Staphylococcus aureus, Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Salmonella typhi, Proteus vulgaris, Shigella flexneri*) and four fungal strains (*Aspergillus niger, Candida albicans, Aspergillus fumigatus, Aspergillus clavatus*). Compound containing electron withdrawing group like chloro, fluoro as substituent on phenyl ring **14M**, **14N**, **14O**, and **14P** showed significant activity against both the gram-positive as well as gram-negative bacteria and compound 12o having electron donating group methoxy as substituent on phenyl ring also showed good activity against both bacterial strains (gram-positive and gram-negative). Compounds **14M**, **14N**, **14Q** depicted significant activity against fungal starins [64].

The antimicrobial activity was evaluated for a series of novel spiro[indole-thiazolidine]spiro[indole-pyran] derivatives by R. Sakhuja *et al*., in vitro with respect to three Gram-positive bacteria (*S. aureus, B. subtilis, and Staphylococcus epidermis*), four Gram-negative bacteria (*E. coli, P. aeruginosa, S. typhi, and K. pneumoniae*). Most of them showed moderate actinity and compound **14R** showed pronounced activity almost equipotent to Ciprofloxacin with respect to Gram-positive and Gram-negative bacteria [65].

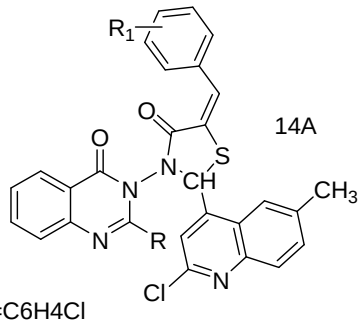
N. H. Metwally *et al.* synthesized many thiazolidinone derivatives. Compound N-(2,3,4,6-tetra-O-acetyl-b-D-glucopyranosyl)-5-[(3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene]-2-thioxo-4-thiazolidinone **14S** exhibited good activity against E. Coli [66].

A.P. Liesen *et al.* synthesized 4-thiazolidinone derivatives and evaluated against variety of pathogens for their antibacterial and antifungal activity. The results showed that derivatives possessed weak antibacterial and antifungal activities compared to standard drugs chloramphenicol and rifampicin for antibacterial activity and ketoconazole for antifungal activity. Compound **14T** showed good activity against *B. Subtilis* [67].

Novel 7-(2-substituted phenylthiazolidinyl)-benzopyran-2-one derivatives was reported by P.M. Ronad *et al.* and were evaluated against various bacterial and fungal strains. The results showed that most of the compounds exhibited good antibacterial and antifungal activity as that of standard antibiotics Ciprofloxacin and Griseofulvin. Compound **14U** found to be the most active derivative [68].

A. Upadhyay *et al.* synthesized N-[(4-oxo-2-substitutedaryl-1,3-thiazolidine)-acetamidyl]-5-nitroindazole derivatives and screened them for antibacterial activity against *E. coli, B. subtilis and S. typhi* and antifungal activity against *A. flavus, P. citrinum and F. oxysporum*. Compounds **14V** and **14W** in which a nitro group was present at ortho and meta positions of the aryl ring, respectively possessed stronger antibacterial and antifungal activity against all tested strains [69].

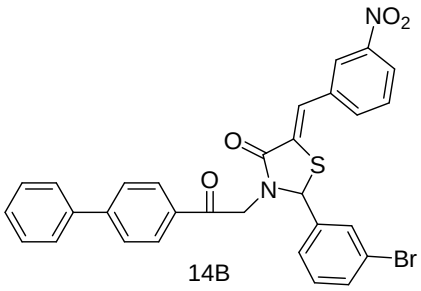
A novel series of 4-thiazolidinones was prepared by N.B. Patel and F.M. Shaikh and were screened for their antimicrobial activity. Compound **14X** revealed highest antibacterial activity against *Escherichia coli* [70].



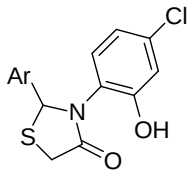
14A

R=C6H4Cl

R1= -2 -Cl, -3 -Cl, -4 -Cl, -2 -NO2, -3 -NO2, -4 -NO2, -2 -OH, -3 -OH, -4 -OH, -4 -CH3, -4 -OCH3, -3,4,5 -(OCH3)3

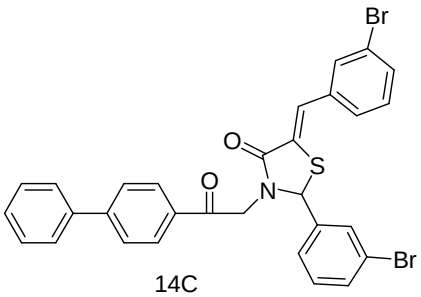


14B

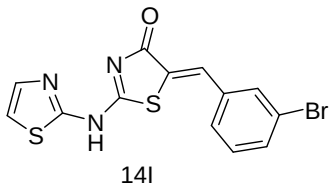


Ar

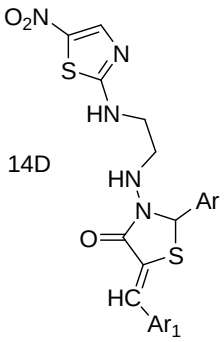
14E	4-methylphenyl
14F	2,4-dimethoxyphenyl
14G	4-hydroxybenzyl
14H	4-methylthiazol-5-yl



14C

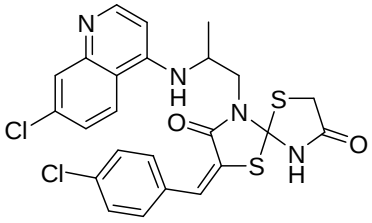


14I

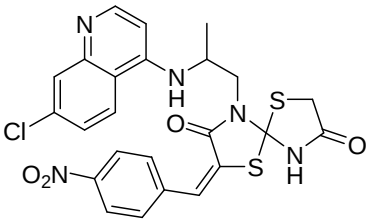


14D

Ar=Ar_1=substituted phenyl ring=C_6H_4, $4ClC_6H_4$, $3ClC_6H_4$, $2ClC_6H_4$, $4BrC_6H_4$, $3BrC_6H_4$, $2BrC_6H_4$,$4NO_2C_6H_4$, $3NO_2C_6H_4$, $2NO_2C_6H_4$, $4CH_3OC_6H_4$, $4CH_3C_6H_4$, $4HOC_6H_4$



14J



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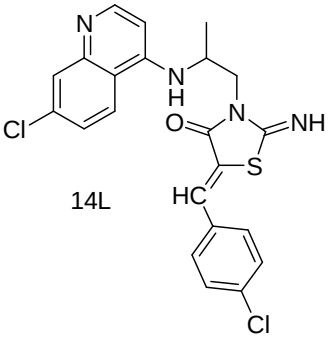

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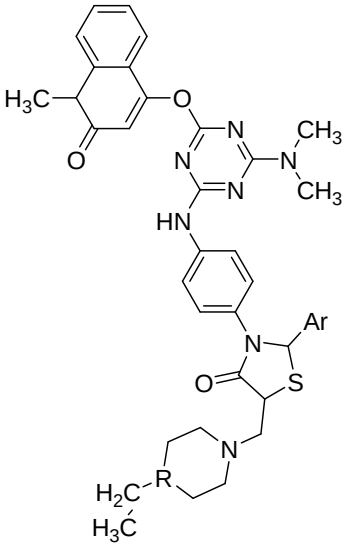

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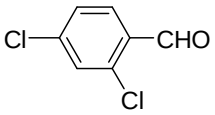
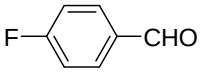
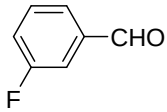
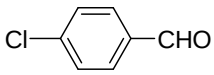
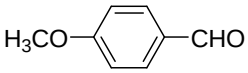
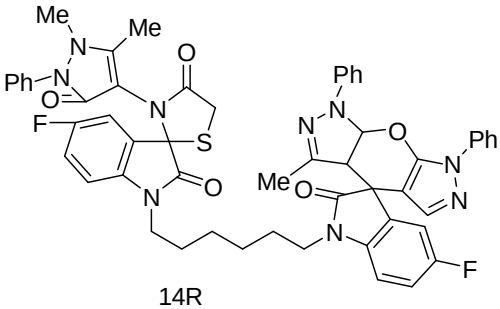
14M	
14N	
14O	
14P	
14Q	



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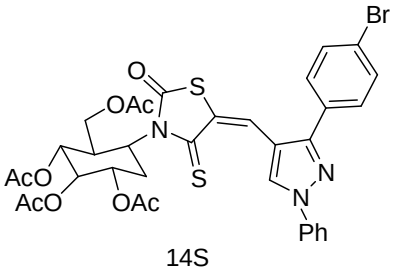

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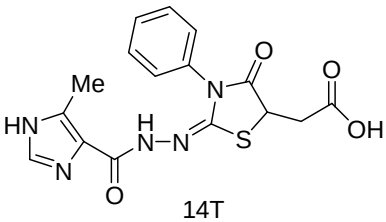

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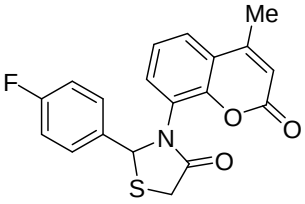

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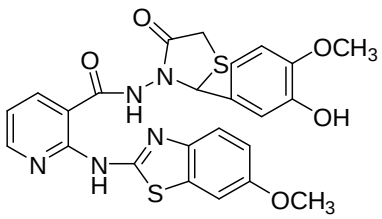

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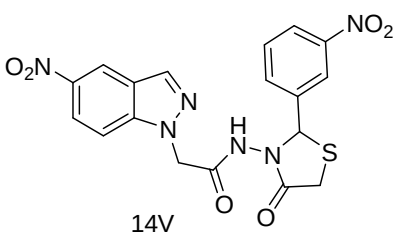

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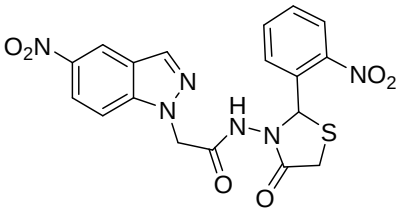

14W

CONCLUSION

Thiazolidinone is a biologically important compound and thus, it attracts various medicinal chemists. In this review, pharmacological activities of various thiazolidinone derivatives has been done.

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