*Section A-Research paper*
**ISSN 2063-5346**

# A brief overview of 4-Thiazolidinone's biological activity, SAR, current advancements, and impending challenges

**Ashutosh Pathak[1], Annie Gupta[2], Arti Gautam[1], Sandeep Arora[2], Dr. Neetu Soni*[1], Dr. Desh Deepak Pandey[3], Dilip verma[4], Shivangi Kushwaha[4], Swati Singh[4], Priyanka Rana[5] , Parul Singh[6]**

1. Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, Allahabad, 211 007 Uttar Pradesh, India.
2. Amity Institute of Pharmacy, Amity University, Sector 125, Noida, Uttar Pradesh – 201303, India.
3. Department of Pharmaceutical Chemistry, City College of Pharmacy Bajha Pratapganj, Faizabad Rd Barabanki, Uttar Pradesh-225001, India.
4. Department of Pharmaceutical Chemistry, Maharana Pratap School of Pharmacy, Mohanlal Ganj Lucknow, Uttar Pradesh-226301, India.
5. Faculty of pharmacy Veer Madho Singh Bhandari Uttarakhand Technical University Dehradun-248007, India
6. Department of pharmacology, Goel Institute of Pharmacy and Sciences Lucknow-226028 , India

**Correspondence to Author:**

**Dr. Neetu Soni**
Department of Pharmaceutical Sciences,
Sam Higginbottom University of Agriculture,
Technology & Sciences (SHUATS), Naini,
Prayagraj, Uttar Pradesh-211007, India
E.mail: neetu.soni@shiats.edu.in

**Abstract**- Saturated Thiazolidinone, which has a carbonyl group on the fourth carbon, has been dubbed the "wonder nucleus" because it exhibits nearly all known biological functions. Many researchers have been interested in exploring this skeleton's ability to be used in a variety of ways due to the diversity in its biological response profile. The current paper is an honest effort to review 4-thiazolidinone's chemistry, synthesis, spectral studies, and applications.

**KEYWORDS:** 4-thiazolidinone, Chemistry, SAR, pharmacological activity

## 1. Introduction

Microbe-based infections are one of the main killers in the world. A significant problem is presented by the limited number of antibiotics that are available for the treatment of illnesses and the ongoing emergence of antimicrobial agent resistance [1]. This is a fundamental component of numerous synthetic medications with a wide range of biological effects, including antimycobacterial effects [2,3]. Thiazolidinones are thiazolidine compounds that contain carbonyl groups at positions 2, 4, or 5 as shown in

**Fig.1,2**. They also contain Sulphur atoms at positions 1 and 3. However, its derivatives are among the moieties that are most commonly researched, and the discovery of its existence in penicillin was the first indication that it existed in nature. The heterocyclic nucleus of 1,3-thiazolidin-4-ones has a Sulphur atom at position 1, a nitrogen atom at position 3, and a carbonyl group at position 4 [4,5]. The thiazole ring, which is a component of vitamin B, penicillin, and antimicrobial thiazoles, is currently well investigated. Reduced thiazole is used to research polypeptides and proteins and appears as structural components in compounds of biological significance.

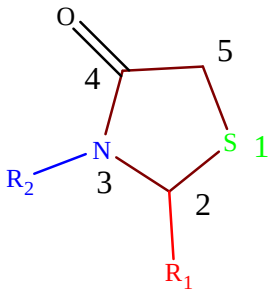



**Fig.1**

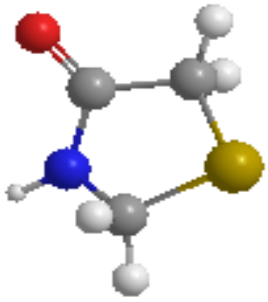


**Fig.2**

### 1.1. Physical Properties 4-Thiazolidinones

The 3-unsubstituted 4-thiazolidinones are typically solids that frequently melt upon decomposition; however, the melting point is lowered by the addition of an alkyl group to the nitrogen. Water is moderately soluble in the 4-thiazolidinones that don't have aryl or higher alkyl substituents [6]. The majority of 4-thiazolidinones are solids; nevertheless, they frequently melt during decomposition due to the alkyl group attached to the nitrogen, which reduces melting temperatures and occasionally results in oily compounds. Thiazolidinones with lower molecular weight and no aryl or higher alkyl substitution are only partly soluble in water. Water can be used to recrystallize 4-thiazolidinones. Water solubility is decreased by substituent addition. Thiazolidinones have a distinctively powerful scent whether they are substituted or not. The introduction of substitutes reduces scent intensity. Thiazolidinones typically lack colour or have a distinctive hue [7]

### 1.2. Molecular Spectra of 4-Thiazolidinones

#### 1.2.1. Infrared Spectra

The 4-thiazolidinones' infrared spectra can be used to determine these compounds' structures. The strong and distinctive carbonyl peak is typically located between 1760 cm-1 and 1655 cm-1. This area does not include a peak for 2-Thionothiazolidine, which is missing a 4-carbonyl group61. 4-Thiazolidinones that have a hydrogen bonded to the nitrogen exhibit absorption in the 3100–3000 cm-1 range, which is indicative of the NH stretching. The thiureide band typically ranges from 1500 to 1450 cm-1. Strong bands are seen for rhodanine derivatives in the 1100–1200 cm-1 range and are categorized as belonging to the C=S group **[8].**

#### 1.2.2. 1H NMR Spectra

4-thiazolidinones' 1H NMR spectra are heavily influenced by the substituents that are present at various locations on the thiazolidine ring. The NMR spectra of 2,3-disubstituted 4-

thiazolidinones has three distinctive peaks, and depending on the nature of the R2, H (2) appears as a singlet in the 5–6 ppm range. Most of the time, Ha and Hb show up as independent doublets in the 3.5–3.9 ppm range. The actual NMR spectra rely on the types of substituents at the C (2) and N (3) locations, or on R1 and R2[9].

### 1.2.3. $C^{13}$NMR Spectra

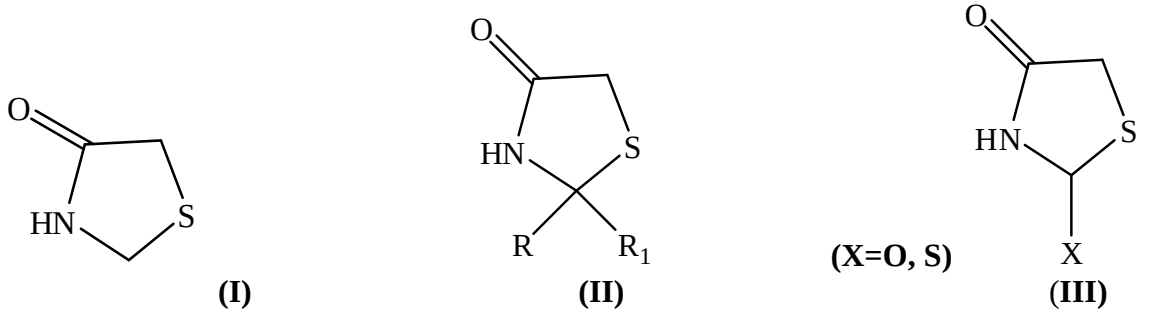
A group of substituted 4-thiazolidinones were explored in CDCl3 by Vogel et al. who examined their 13C NMR spectra. On the basis of the C, H spin coupling constants over two and three bonds, several constitutional isomers were discriminated, and the configuration of trisubstituted exocyclic C=C was determined. [10]

### 1. 2.4 Reactions of 4-Thiazolidinones

The nucleus of 4-thiazolidinone is moderately reactive and goes through several changes. Below are some of these responses highlighted. Numerous attempts have been made at the aldol condensation process of the methylene group at position-5. Thiazolidinones have a nucleophilic carbon atom at position 5 that has the ability to attack an electrophilic core. The reaction takes place when an attacking species of 4-thiazolidinone base and anion are present. The ease of formation of anion and hence the degree of nucleophilic activity is dependant not only on the electron withdrawing effect of the adjacent carbonyl group but also on the presence of other electron withdrawing groups at position-2. The product of the reaction contains α,β-unsaturated carbonyl group. Different 2-thiono-4-thiazolidinones have been reported39,71 to undergo aldol condensation reaction with a variety of aliphatic, aromatic and heterocyclic aldehydes. 5-unsaturated derivatives (10), which are very useful synthetic reagents, were obtained in good yields. The reactions were mostly carried out in the presence of anhydrous sodium acetate in benzene or acetic acid. [11]

### 1.2.5. Chemistry of 4-Thiazolidinones

The chemistry of 4-thiazolidinones was reviewed in depth by Brown in 1962 and by Newkome and Nayak in 1977. 4-Thiazolidinones are derivatives of thiazolidine with a carbonyl group at the 4-position (I). 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. Variations in the substituents attached to the nitrogen atom and the methylene carbon atom are possible for the structures represented by (II) and (III)as shown in **Fig.3**. Thiazolidinone is considered as a biologically important active scaffold that possesses almost all types of biological activities. [12-13]




**(I)** **(II)** **(III)**

**Fig. 3**

4-Thiazolidinones are one of the most intensively investigated classes of aromatic five membered heterocycles. 4-Thiazolidinones are the structural units of biological and medicinal importance. Numerous methods for the synthesis of thiazolidinones and also their diverse reactions offer enormous scope in the field of medicinal chemistry. Thiazolidinone, a saturated form of thiazole with carbonyl group on fourth carbon, has been considered as a magic moiety (wonder nucleus) which posse almost all types ofbiological activities. This diversity in the biological response profile has attracted the attention of many researchers to explore this skeleton to its multiple potential against several activities**.** The carbonyl group of 4-thiazolidinone is highly unreactive. But in few cases 4-thiazolidinone on reaction with Lawesson's reagent gives corresponding 4-thione derivatives [14-15]

### 1.2.6. Preparation of thiazolidinones derivatives

Several methods for the synthesis of 4-thiazolidinones are widely reported in the literature. The main synthetic routes to 1,3-thiazolidin-4-ones involve three components that is an amine, a carbonyl compound, and a mercapto-acid. The classical synthesis reported can be either a one-pot three-component condensation. The reactions begin by formation of an imine (the nitrogen of amine attacks the carbonyl of aldehyde or ketone), which undergoes attack by generated sulfur nucleophile, followed by intramolecular cyclization on elimination of water as shown in **Fig.4** [16].

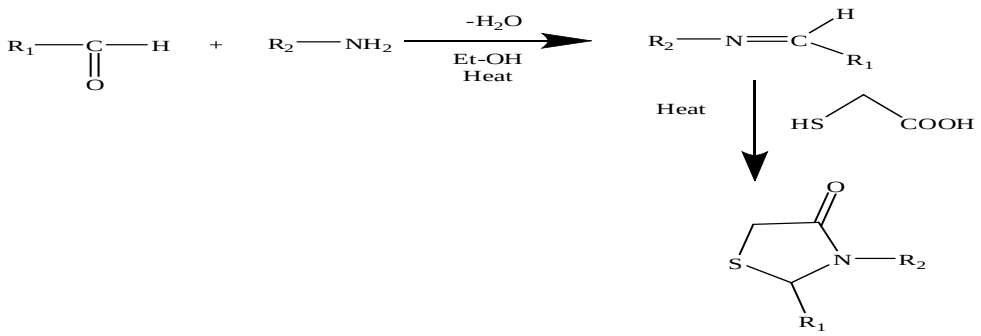



**Fig. 4**

Common synthetic route for the synthesis of 4-thiazolidinone derivatives

### 1.2.7. Mechanism of thiaozolidin-4-one ring formation

The group –CH=N- has two reaction centres, one at the methine carbon atom and the nucleophilic center at the nitrogen atom. Through this, azomethine bases can react with molecules containing a replaceable hydrogen atom. Thus, the reaction proceeds by the attack of mercapto acetic acid upon the –C=N- group with the thioglycolic acid (SCH2 COOH) adding to the carbon atom followed by the capture of proton by nitrogen and subsequent cyclization. as shown in **Fig.5** [17-18]

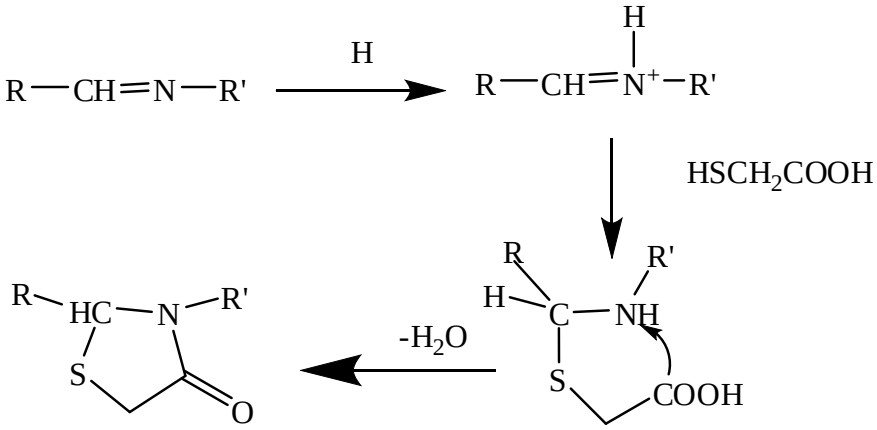


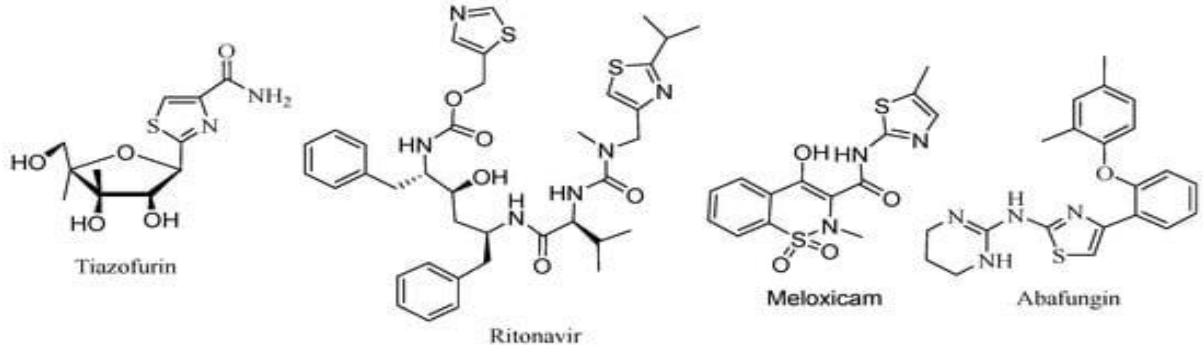

**Fig. 5**
**Mechanism of thiaozolidin-4-one ring formation**

## 2. Biological importance

Thiazolidinones are the structural units of biological and medicinal importance.4-thiazolidinones and their derivatives are an important class of compounds in organic and medicinal chemistry. The 4-thiazolidinone ring system is a core structure in various synthetic pharmaceutical agents, displaying a broad spectrum of biological activities such as anti-tubercular, anti-convulsant, anti-cancer, anti-fungal, anti-inflammatory and analgesic etc as shown in **Fig.6**. Numerous reports have highlighted their chemistry and uses. It has also been reported in literature that certain compounds bearing 4-thiazolidinone nucleus possess various activities as shown in **Fig.7**,**8** [19].

- Antibacterial and antifungal activity
- Anti-inflammatory activity
- Antituberular activity
- Antidiabetic activity
- Antiviral activity
- Antiarrhythmic activity
- Anticancer activity
- FSH receptor agonist and Muscarinic receptor 1 agonist


**4-thiazolidinone nucleus possess various activities (Fig. 6)**



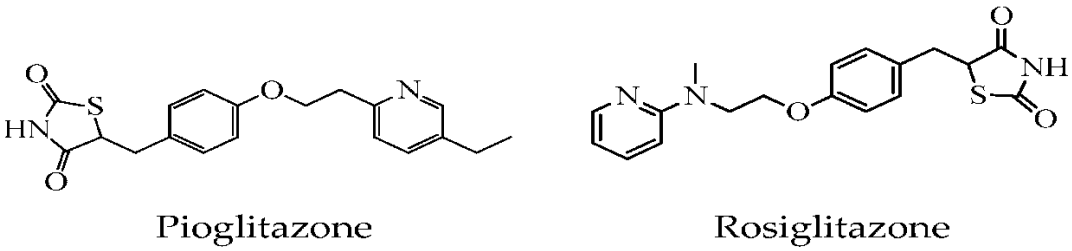
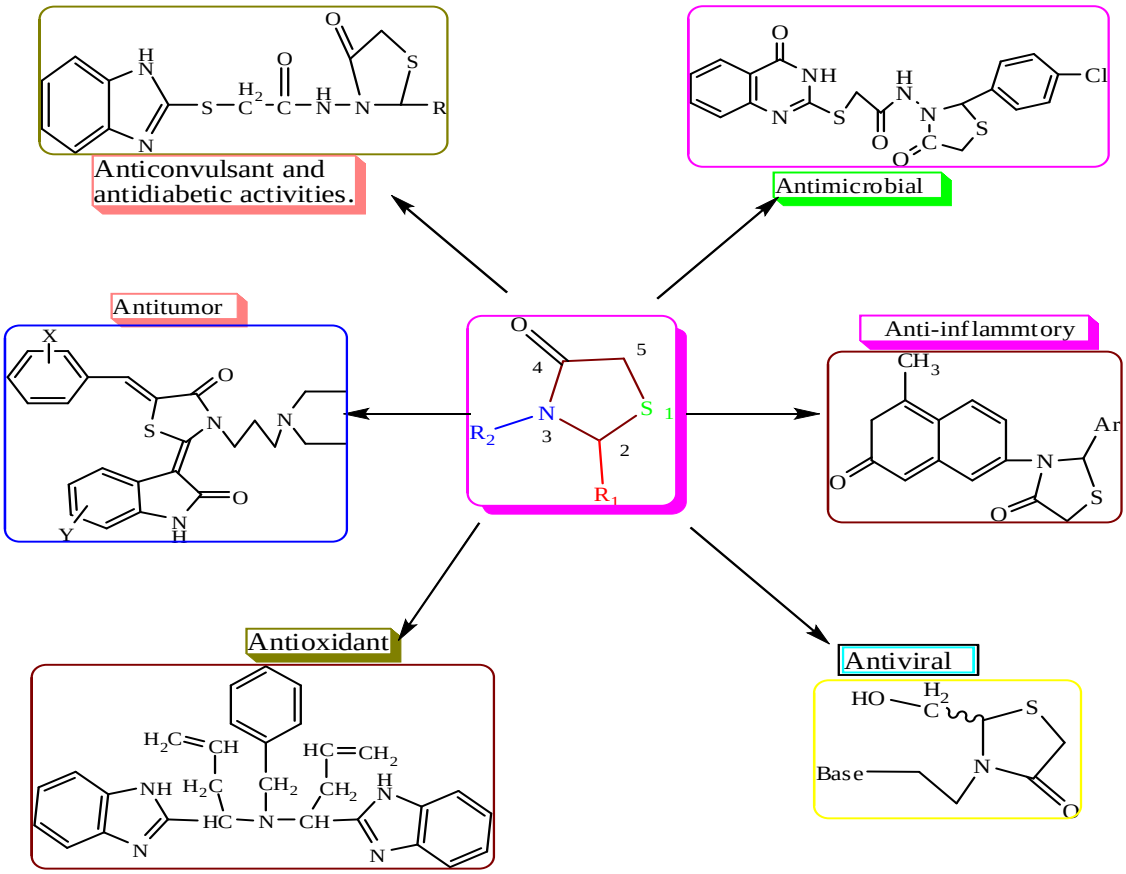



**Fig. 7**
**Prescribed medications with thiazole scaffold**




**(Fig. 8) 4-thiazolidinone, a multifunctional nucleus.**

### 2.1. Anti-inflammatory and analgesic activity

**Chawla *et al* 2023,** reported 4-thiazolidinone derivatives that were produced in three successive phases utilising a standard approach. Through spectrophotometric examination, the compounds' structural identification was discovered. The created chemicals were also tested for their ability to fight cancer, inflammation, and antioxidants. All of the synthetic derivatives had fair to moderate antioxidant properties, with FP7 and FP10 showing the greatest scavenging activity as shown in **Fig.9** The carrageenan-induced rat paw oedema technique was used to test the in vivo anti-inflammatory activity, and the compounds FP4 and FP7 had the highest levels of inhibition. Compounds as shown in **Fig.9** were discovered to be

the most effective analogues against the tested cell lines after the synthesised analogues were evaluated for in vitro antitumor activity over MOLT-4 and EAC cell lines. Molecular docking research was done using Auto Dock 4.2.6**. [20].**

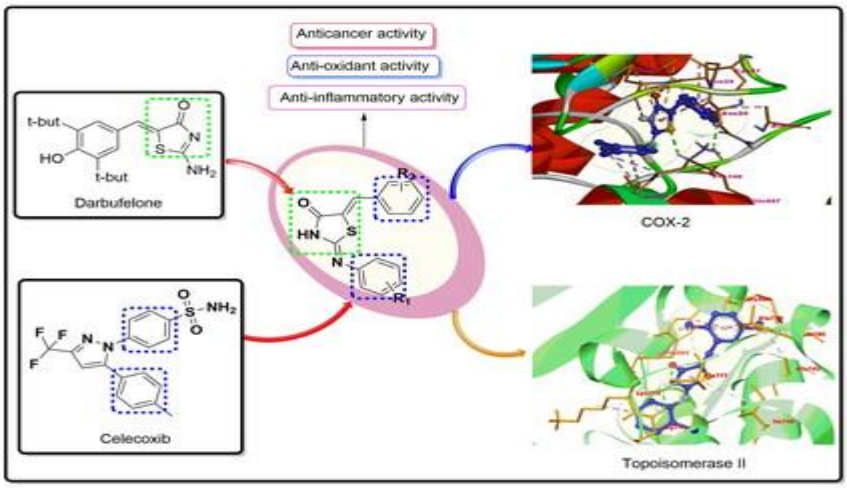



**Fig.9**

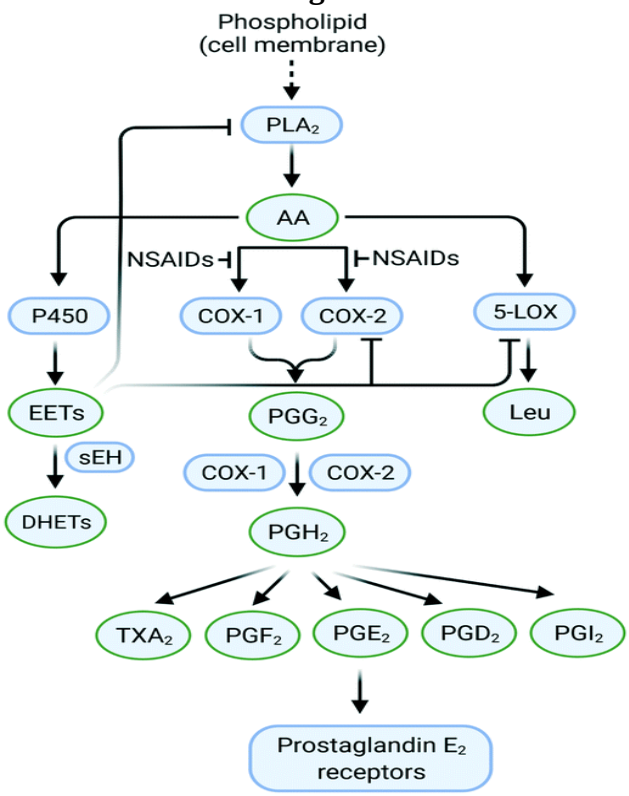



**Fig.10**

Pathways leading to inflammation and its suppression by COX-2, 5-LOX, and sEH targeting. using BioRender.com to create

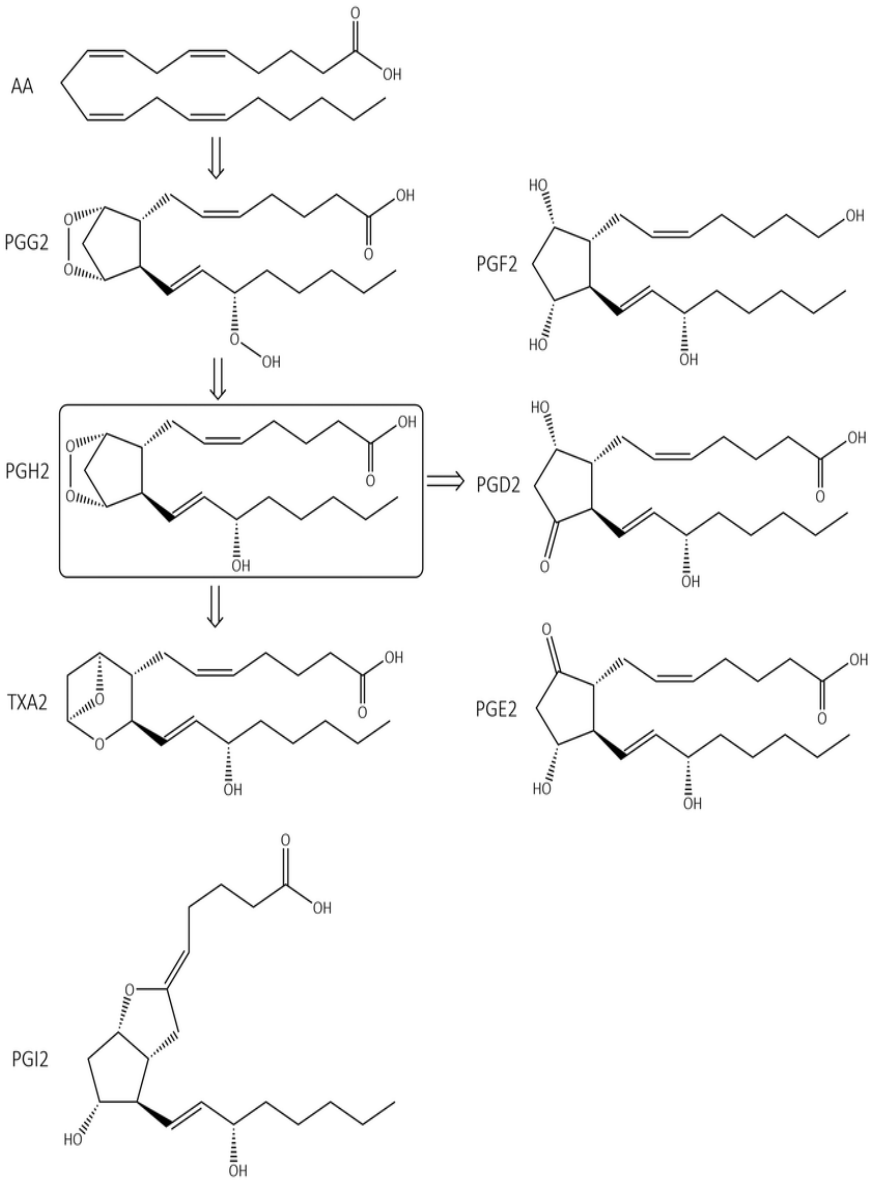



**Fig. 11** Arachidonic acid (AA) cascade. PG = prostaglandin, TX = thromboxane. As reported in Ahmad *et al* 2022 [21]

**Haroun *et al* 2023** reported new anti-inflammatory drugs with improved gastrointestinal profiles. He reported that anti-inflammatory properties of thiazolidinones based on 4-methylthiazole. anti-inflammatory activity, evaluated pharmacological action, ulcerogenicity, and cytotoxicity of a series of 5-adamantylthiadiazole-based thiazolidinone derivatives based on these observations. The substances had moderate to outstanding anti-inflammatory efficacy, according to the in vivo anti-inflammatory activity. The four compounds shown in **Fig.12** were more potent than the control medication indomethacin (47.0%), with relative potencies of 62.0, 66.7, 55.8 and 60.0%. The COX-1, COX-2, and LOX enzymatic assay was carried out to ascertain their potential mode of action [22].

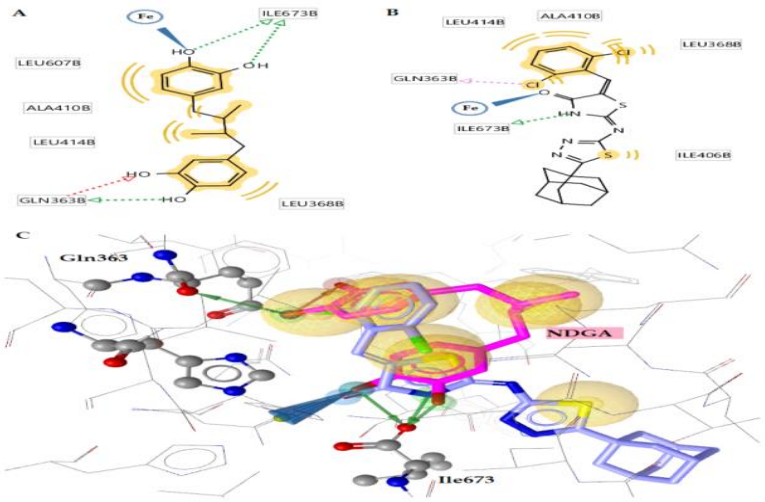



**Fig. 12**

**Desai *et al* 2023** reported antibacterial and antifungal properties of a series of 4-thiazolidinone- which is based on5-arylidene hybrids, they were developed and synthesised. Several spectrum approaches, including IR, 1H NMR, 13C NMR, and mass spectroscopy, were employed to determine the structure of a unique synthesised hybrid. To assess antibiotic activity, four bacterial strains—two gram-negative (Escherichia coli and Pseudomonas aeruginosa), two gram-positive (Staphylococcus aureus and Streptococcus pyogenes), and one fungal (Candida albicans)—were employed. Due to their MIC values of 62.5 g/mL against the tested bacterial strains (S. pyogenes, P. aeruginosa, and E. coli, respectively) [23].

**Haroun *et al* 2022** reported new compounds that are safer and have different molecular targets than those currently being used in clinical settings. This study sought to identify a group of thiazolidinones based on benzothiazoles that have lipoxygenase (LOX) inhibitory activity as a mechanism of anti-inflammatory effect. Anti-inflammatory effect was assessed using a carrageenan-induced mouse foot paw oedema experiment, and LOX inhibition was investigated using the conversion of sodium linoleate to 13-hydroperoxylinoleic acid. Molecular docking research was carried out with Auto Dock 4.2. The anti-inflammatory activity of the aforementioned compounds was estimated to be between 18.4% and 69.57%, indomethacin (47%). Additionally, compound #3 had the strongest LOX inhibitory efficacy.[24]

**Haroun *et al* 2022** reported prescribed medications with thiazole scaffold and also discuss (PASS and docking) led to the selection of seventeen compounds for biological assessment., PASS predictions enable us to pick molecules with favourable activity as efficiently as possible. Prediction suggests that these substances could be used as possible anti-inflammatory drugs. These findings led to the selection of potential compounds, which were then tested for their ability to reduce inflammation. The most promising substitution compounds were 4-NO2, 2,3-di-Cl, 3-Br as shown in Fig.13-14 Three of the most active compounds were tested in vitro for their ability to inhibit COX-1/COX-2 and LOX, and the results showed that they are effective COX-1 inhibitors with IC50 values that are better than

those of the reference compound Naproxen (IC50 = 40.10 M), which is in line with the findings of our predictive molecular approach [25].

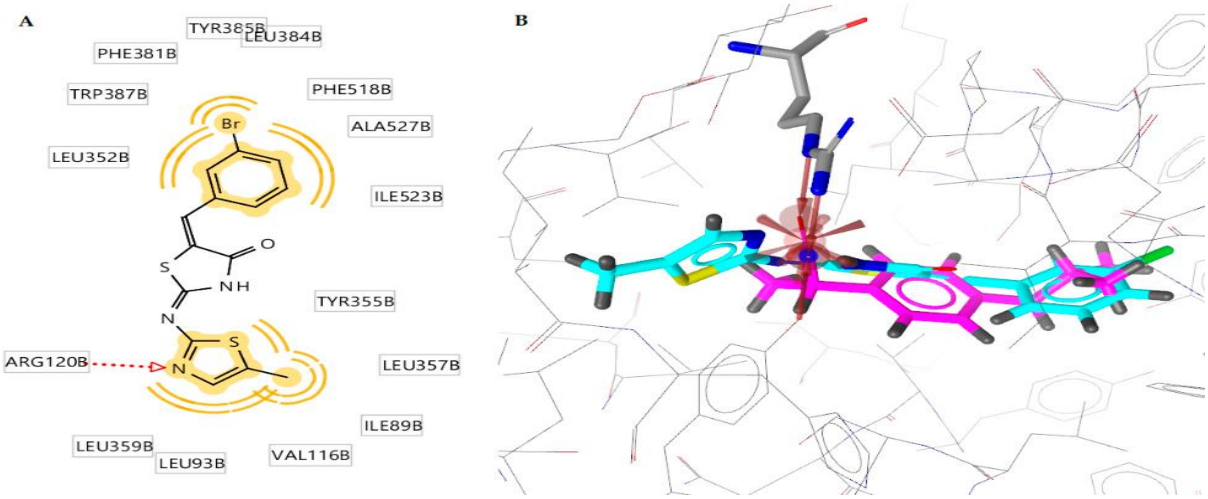



**Fig.13**

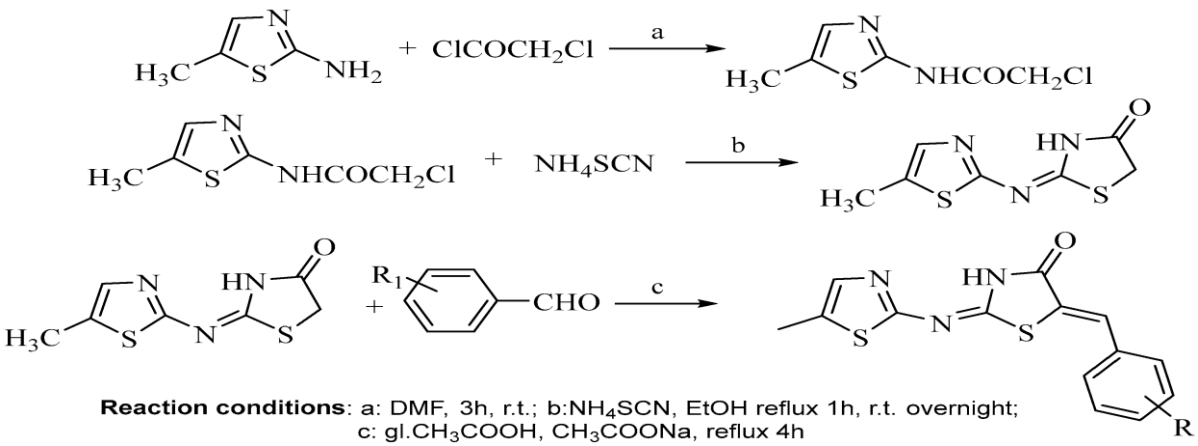



**Fig.14**

**Karapetyan *et al* 2022,** reported Environmentally friendly and without catalyst Two methods have been devised for the synthesis of compounds with iminodihydrofuran and thiazolidinone rings that have been functionalized as shown in **Fig.15** Thiourea linker was employed to join a thiazolidinone scaffold to iminodihydrofuran. The techniques provide for good to exceptional yields of the polyheteroconjugated compounds while being affordable, easy, and operationally straightforward.[26]

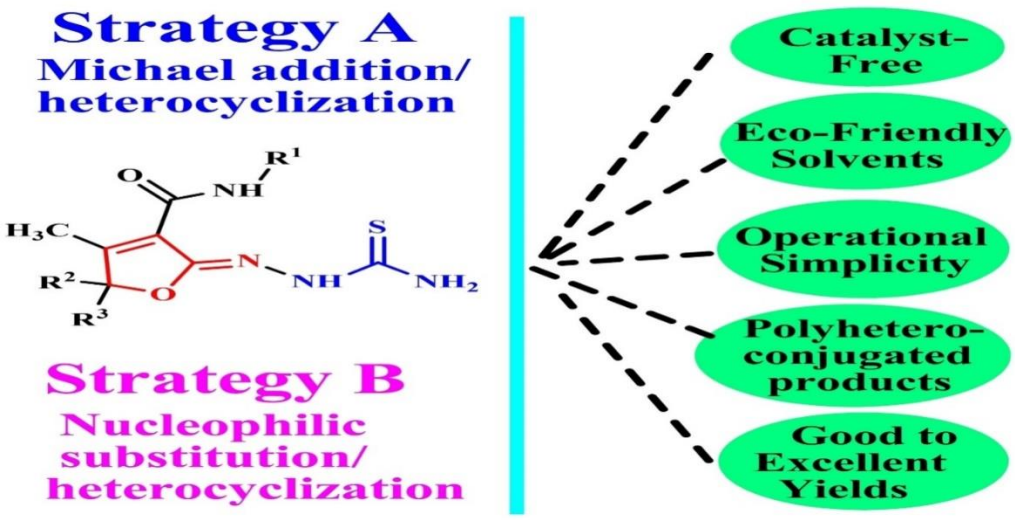



**Fig.15**

**Abd El-Karim *et al* 2021** reported newly synthesised compounds underwent in-vivo anti-inflammatory and ulcerogenic testing using indomethacin, celecoxib, and diclofenac as reference medicines. The compound Fig.16 seemed to be the most promising choices since they produced anti-inflammatory action that was quick to start acting and lasted a long time, as well as a positive GIT safety profile. The later derivatives also underwent molecular docking studies to explain their binding affinities and their proteins ‘as shown in **Fig.16** [27].

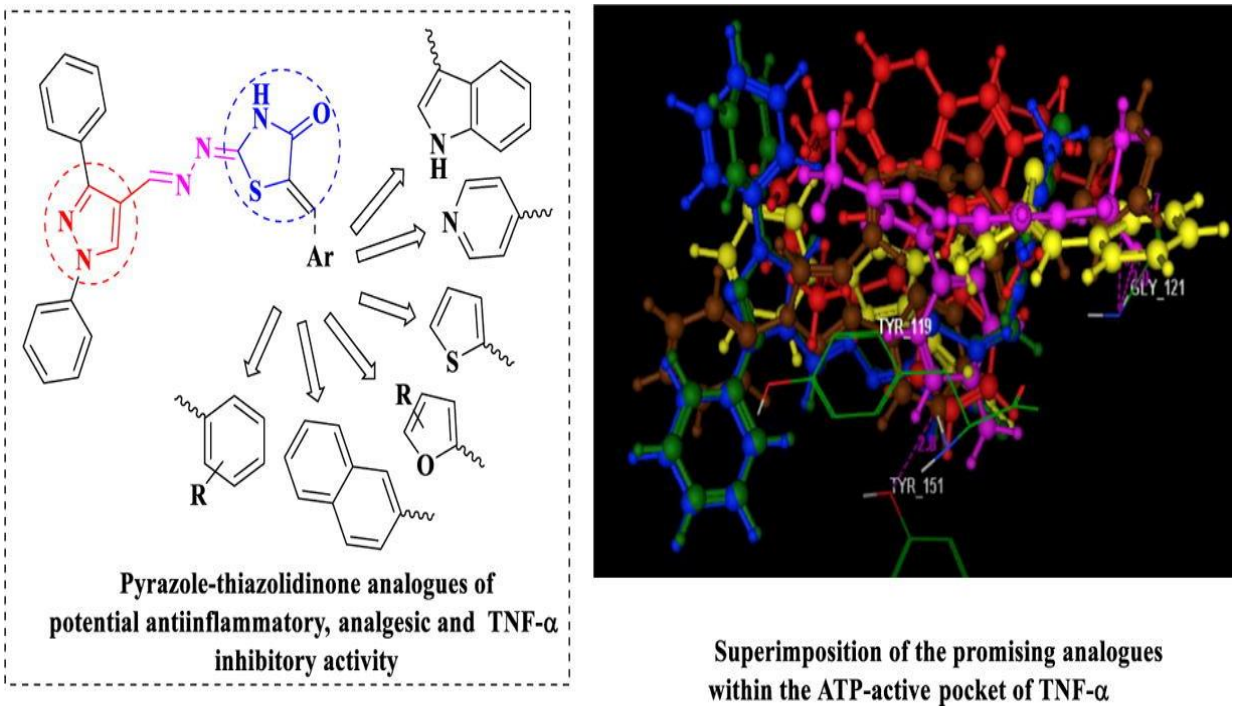



**Fig. 16**

**Shawky *et al* 2020** reported that two novel series of pyrrolizine-5-carboxamides were created, and their anti-inflammatory and anticancer properties were examined. With a selectivity index in the range of 1-258, the novel compounds showed strong cytotoxicity (IC50 = 0.10-22.96 M) against three cancer cell lines (MCF-7, A2780, and HT29). Additionally, these substances demonstrated notable anti-inflammatory action (18.13-44.51% suppression of inflammation), which was mediated by COX-1/2 inhibition with a preference for COX-2 inhibition.The investigation of SAR showed that the aliphatic side chain and 4-thiazolidinone moiety at C6 of the pyrrolizine nucleus had favourable effects on cytotoxicity, while the (hetero)aromatic substituents increased the anti-inflammatory actions. The IC50 values required to suppress the proliferation of cancer cell lines were greater than those needed to inhibit COX-2. Synthesise compounds were also shown to inhibit a number of kinases in mechanistic investigations. Docking tests showed that the novel chemicals fit well into COX-1/2. In addition, compounds in **Fig.17** showed greater CDK2 affinities than CAN508. In conclusion, the facts above identify these substances as promising anti-inflammatory [28].

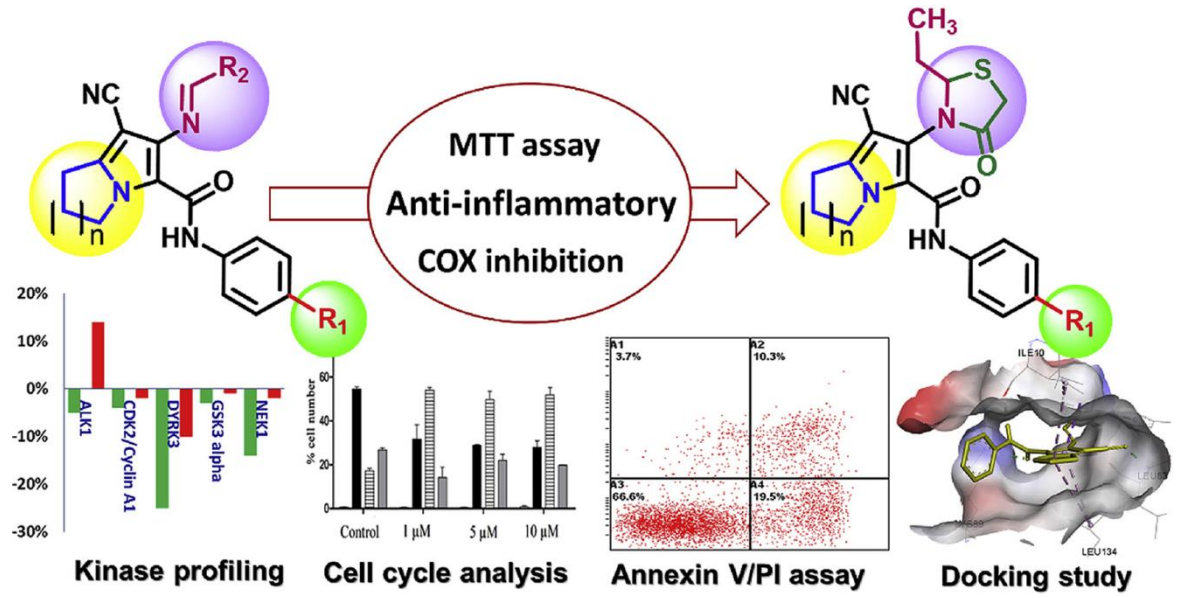



**Fig.17**

**Adnan *et al* 2019** reported Two new 2-methyl benzoimidazole and substituted thiazolidines compounds were created, produced, and assessed as possible COX-2 [cyclooxygenase-2] inhibitors. The synthetic compounds were identified based on their spectrum FTIR, 1H-NMR, and physical characteristics. Ibuprofen [10mg/kg i.p.] was chosen as the reference ligand, and the newly synthesised compounds were tested in vivo for their antiinflammatory effects utilising the egg-white induced paw edoema technique in comparison to the impact of propylene glycol 50%v/v [control group]. Comparing new compounds to ibuprofen as a reference medicine, new compounds demonstrated a much stronger in vivo antiinflammatory efficacy. [29]

**Abdellatif KR, et al 2019**, reported that In two novel series that we created, thiazolidindione derivative or thiazolidinone derivative served as the anti-diabetic moiety, while the pyrazole ring with vicinal diaryl rings served as the selective COX-2 moiety. The two moieties were coupled together using methylene or methylenehydrazone functionality. The two series were assessed for their anti-diabetic activity, ulcerogenic liability, and COX inhibition; were also tested in vitro against α-glucosidase and α-glucosidase, as well as in vivo hypoglycaemic as shown in **Fig.18** [30].

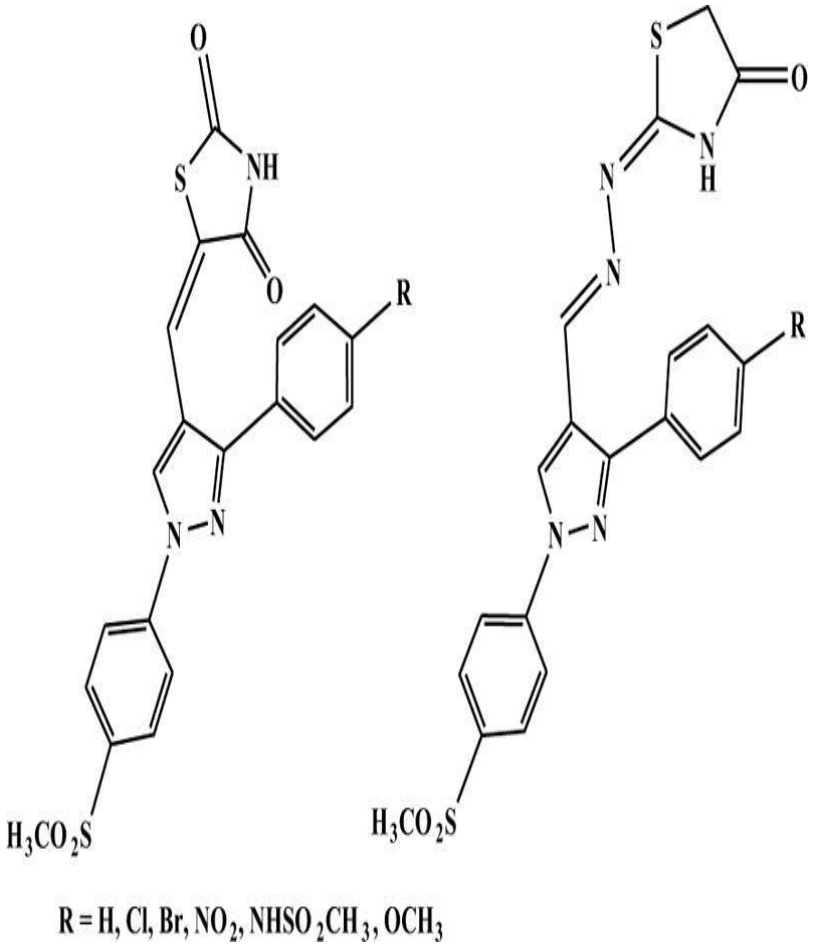
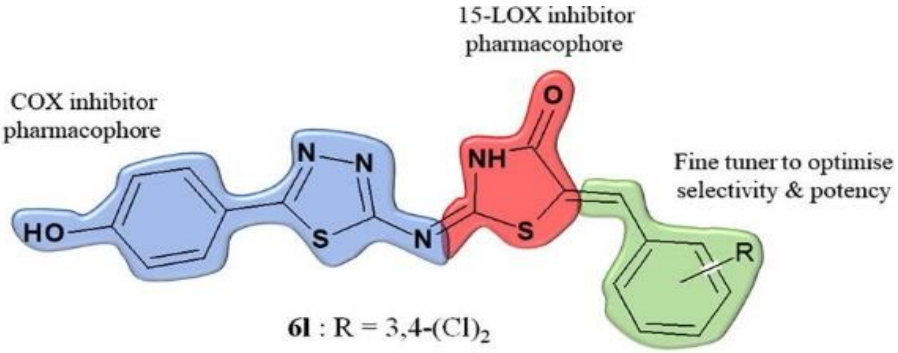



**Fig.18**

**Omar *et al* 2018** Selective inhibition of 15-lipoxygenase (15-LOX) and cyclooxygenase-2 (COX-2) may be a useful approach for reducing inflammatory illnesses while minimising adverse effects related to present anti-inflammatory medications. In the current work, a variety of thiadiazole-thiazolidinone hybrids carrying 5-alk/arylidene as dual inhibitors of these enzymes are synthesised, thoroughly characterised, and biologically assessed. Our strategy was to combine pharmacophores with significant anti-inflammatory properties into a single molecular framework. Effectively produced 4-thiazolidinone as shown in Fig.19 was obtained by chlroacetylating and cyclizing 5-(4-hydroxyphenyl)-1,3,4-thiadiazol-2-amine. The final compounds as shown in Fig.19 resulted from the Knovenagel condensation. Assays for the in vitro inhibition of COX-1/COX-2 and 15-LOX on these drugs were performed.

Compounds as shown in Fig. 18 having promising potency and selectivity (IC50 = 70-100 nM) [31]




| | COX-2 $IC_{50}$ | Selectivity index | 15-LOX $IC_{50}$ |
|---|---|---|---|
| **6l** | **70 nM** | **220** | **11.8 µM** |
| **Celecoxib** | 49 nM | 308 | - |
| **Zileuton** | - | - | 15.6 µM |

**Fig.19**

**Liaras *et al* 2018** reported Numerous naturally occurring physiologically active chemicals, as well as manufactured molecules with a variety of pharmacological properties, contain thiazole and thiazolidinone moieties. The biological activity of several thiazole and thiazolidinone compounds as COX-1/COX-2 and LOX inhibitors is the main topic of this review.[32]

**Apostolidis *et al* 2018** reported new derivatives, 5-arylidene-2-(1,3-thiazol- 2-ylimino)-1,3-thiazolidin-4-ones **(Fig.20)** as anti-inflammatory agents. The structural variations were selected by introducing, at the 5 positions of thiazolidinone moiety, different arylidene substituents that author recently properties as hydrophobic and steric. The comparison of 4-Cl derivatives showed highly significant inhibition compared to the corresponding 4-$CH_3$ substituted derivatives. Good (Cox-1/Cox-2) inhibitory activity was exhibited by 5-(4-(chlorobenzylidene)-2-(4-methyl-1,3-thiazol-2-ylimino)-1,3-thiazolidin-4-one. The protection ranged up to 67.3%, for 5-(4-(dimethylamino) benzylidene)-2-(1,3-thiazol-2-ylimino-1,3-thiazolidin-4-one. while the reference drug, indomethacin exhibited 47% protection at an equivalent dose. Compound **Fig.21** is the most potent [33].

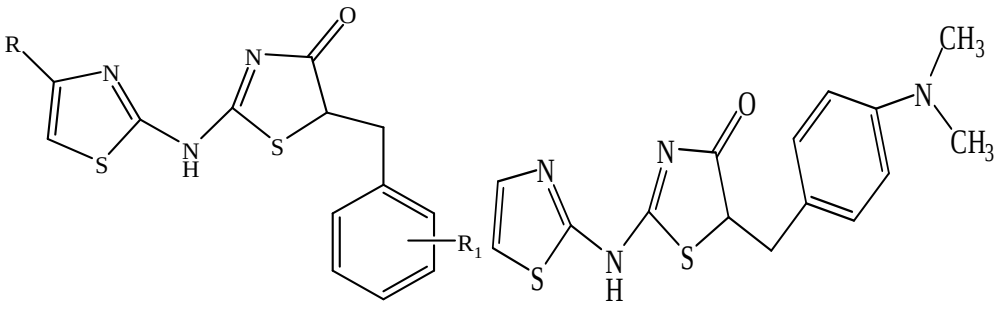



**Fig.20** **Fig. 21**

**Ottanà *et al* 2017** also reported substituted thaizolidinone as anti-inflammatory agents as shown in **Fig.21** [34].

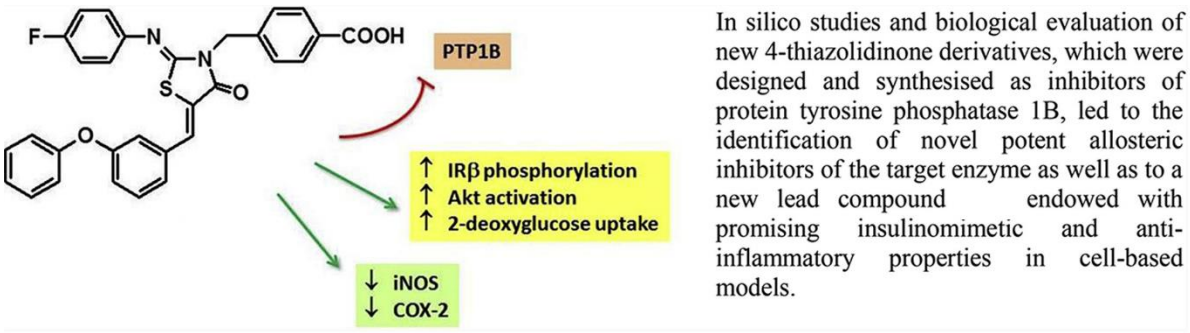



**Fig.22**

**Suthar *et al* 2013** synthesized quinolone substituted thiazolidin-4-ones **as shown in Fig .** by cyclocondensation of m-phenylenediamine and nucleophilic attack of thiol on imino carbon followed by intramolecular cyclization by loss of water. Compound possessing 4-nitrophenyl substitution on thiazolidinonemoiety confers maximum anti-inflammatory activity followedby 3-(4-methyl-2-oxo-1,2-dihydroquinolin-7-yl)-2-(2-nitrophenyl) thiazolidin-4-one as shown in **Fig.22, 23** compound bearing 2-nitrophenyl substitution. All compounds showed excellent anti-inflammatory and anticancer activity [35].

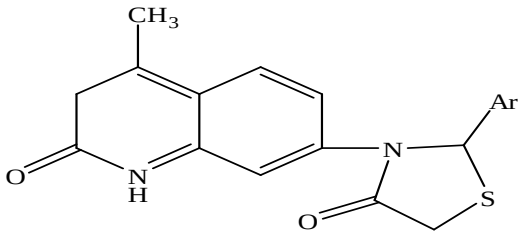



**Fig.23**

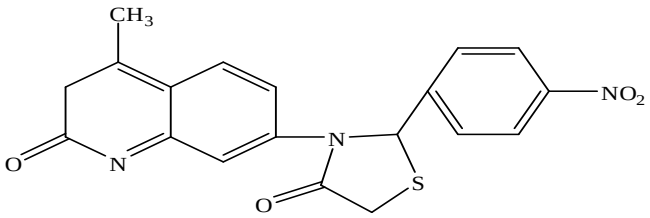



**Fig.24**

**Kumar *et al* 2007** reported some new 3-[4-(p-chlorophenyl)-thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)–aminomethyl]-6-bromoquinazolin-4-ones Fig.24 as anti-inflammatory agents. compound **Fig.25** which was substituted with chloro group at2$^{nd}$ position of phenyl ring, showed almost equal anti-inflammatoryactivity to that of phenylbutazone at 50 mg/kg. Compound **Fig.26,27** with a substitution of bromineon both the aromatic rings showed percentage inhibition of44.59 and 55.73 at 2 and 4 h, respectively. [36]

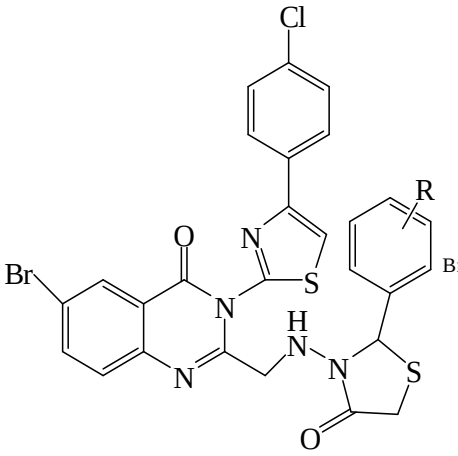


**Fig.25**

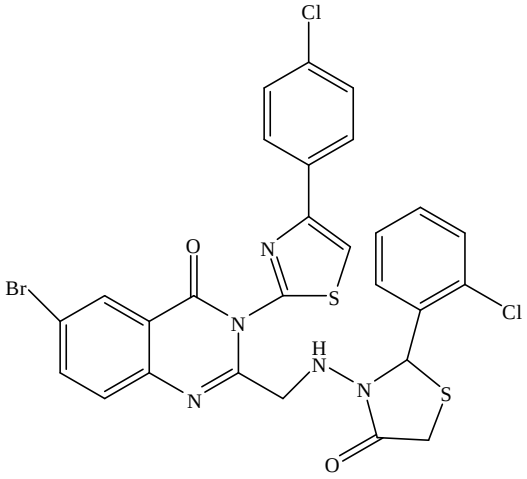


**Fig.26**

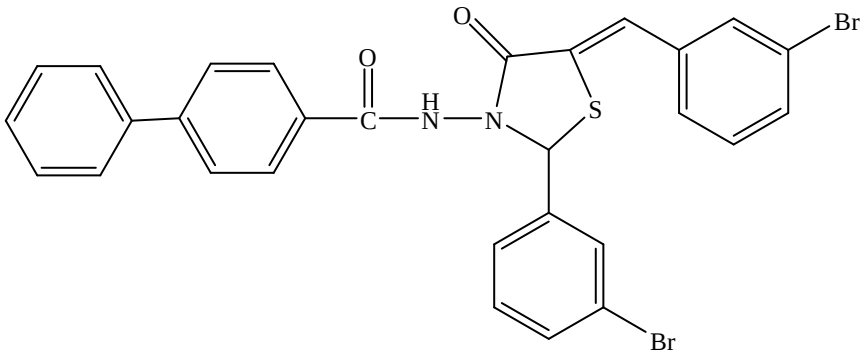


**Fig.27**

**Amin et al 2010** reported novel series of spiro [(2H,3H) quinazoline-2,10- cyclohexan]-4(1H)- one derivatives. These compounds were evaluated for their antiinflammatory, ulcerogenic and analgesic activities. Compound Fig.27 with 2-thiophene substitution at C-2 of thiazolidinone showed anti-inflammatory activity [37].

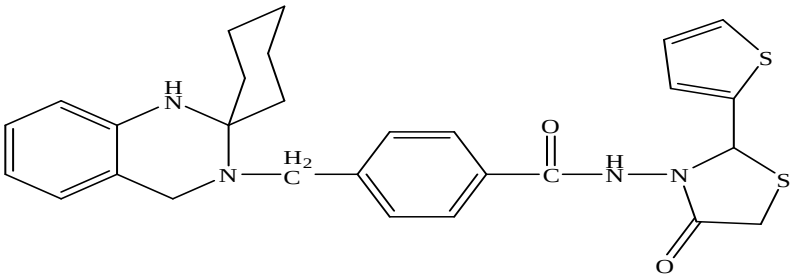


**Fig.28**

**Vigorita *et al* 2001**, reported synthesis and structure-activity connections of a new series of 3,3′-(1,2-ethanediyl)-bis[2-aryl-4-thiazolidinones] that are 2R,2′R/2S,2′S and 2R,2′S-meso. Carrageenin-induced paw edoema was used to test for anti-inflammatory activity, while hot plate and acetic acid writhing tests on rats were used to test for analgesic effectiveness. In comparison to indomethacin and phenylbutazone, all drugs showed ulcerogenic effects and acute toxicity at substantially lower levels. Comparing their pharmacological characteristics, meso isomers outperformed their racemate counterparts. The aryls' methoxy substitution

patterns on stereogenic carbons are often those with the best pharmacological profiles.Rac 2R,2′R/2S,2′S and 2R,2′S mesoform synthesis and SARs are described. They showed stereoselective anti-inflammatory abilities and favourable safety profiles as shown in **Fig.29[38]**

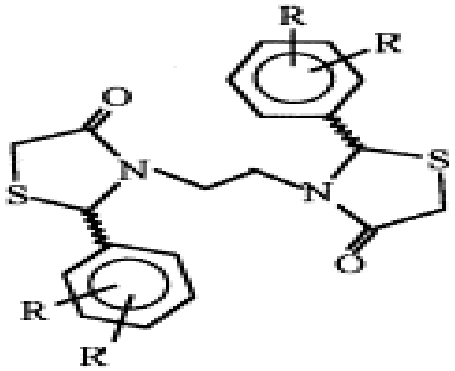
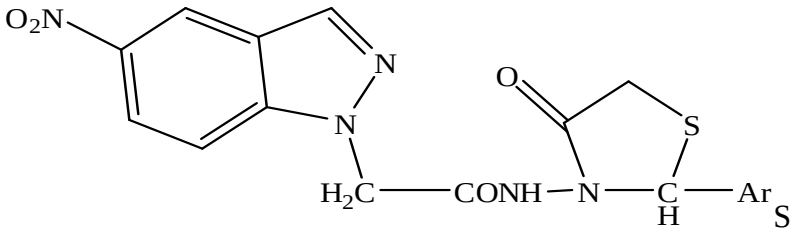


**Fig.30**

## 2.2. Antibacterial and Antifungal

Thiazolidinones with C-2 and N-3 substituted positions, possess diverse degrees of inhibition against bacteria and fungi. The SAR studies of thiazolidinone derivatives showed that they are more effective on gram-negative bacteria as compared to gram-positive bacteria. Upadhyay *et al* 2010 synthesized some newN-[(4-oxo-2-substituted aryl -1, 3-thiazolidine)-acetamidyl]-5-nitroindazoles **Fig.31** by conventional and microwave assisted methods. The synthesized compounds were evaluated for their antimicrobial activity against *Escherichia coli,Bacillus subtilis* and *Salmonella typhi* at 50 and 100 mg/ml concentrations and antifungal activity *against Aspergillus flavus, Penicillium citrinum*and *Fusariumoxy sporum* at 50 and 100 mg/ml concentrations by filter paper disk technique (MIC 11 and 10 mg/ml). The compounds N-[{4-oxo-2-(2-nitrophenyl)-1,3-thiazolidine}-acetamidyl]-5-nitroindazole and N-[{4-oxo-2-(3-nitrophenyl)-1,3-thiazolidine}-acetamidyl]-5-nitroindazole showed the maximum antibacterial activity against Escherichia *coli* and antifungal activity against *Fusarium oxysporum* (MIC 9 and 8 mg/ml). Most of the analogues showed significant antimicrobial activity [39].



Ar = $C_6H_5$, 2-$NO_2C_6H_4$, 2-$OHC_6H_4$, 3-$NO_2C_6H_4$, 2-$ClC_6H_4$, 2-$CH_3OC_6H_4$, 4-$ClC_6H_4$,

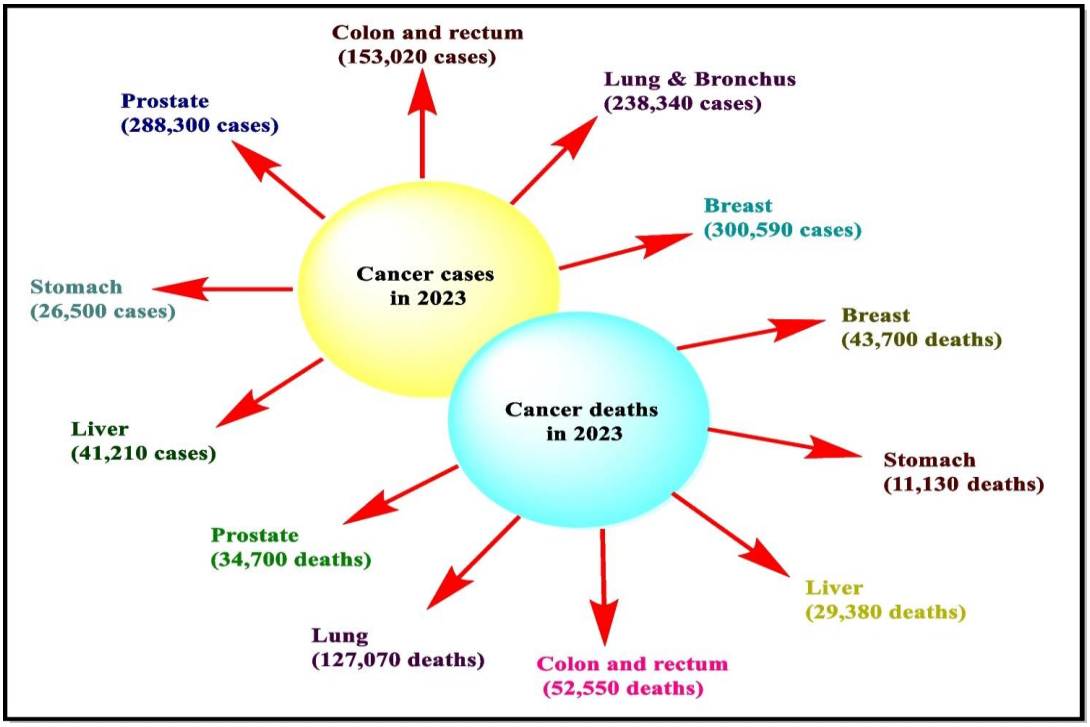



**Fig.31**

2.3. Anticancer activity

Gornowicz *et al* 2023 reported Chemotherapy and immunotherapy are still used together in anticancer treatment regimens. Combining anti-HER2 antibodies with novel 4-thiazolidinone-bearing hybrid molecules may be a potential approach for treating patients with gastric cancer who have been shown to exhibit the human epidermal growth factor receptor 2 (HER2). The study's goal was to create a novel 4-thiazolidinone derivative (Les-4367) and look into how it interacts with pertuzumab or trastuzumab in combination to treat human AGS gastric cancer cells. We looked at the antiproliferative potential and viability of AGS cells. It was also assessed how the evaluated monotherapy and combination therapies affected apoptosis and autophagy. The ELISA method was also used to show the quantities of metalloproteinase-2 (MMP-2), intercellular adhesion molecule 1 (ICAM-1), pro-inflammatory, and anti-inflammatory cytokines [39]

vasechko et al 2023 reported a set of 11 replacements 9-hydroxy-3,5,10,11-tetrahydro-2H-benzo[6,7] thiochromeno[2,3-d][1,3]thiazole-2,5,10-triones Through a hetero-Diels-Alder reaction involving 5-ene-4-thioxo-2-thiazolidinones and 5-hydroxy-1,4-naphthoquinone (juglone), 3.1-3.13 were created. Spectral information and a single-crystal X-ray diffraction study were used to determine the structure of recently synthesised substances. The synthesised substances were examined on a panel of cell lines that represented several cancer types, along with normal and pseudonormal cells, peripheral human blood lymphocytes, and normal and pseudonormal cells. The most potent derivative, compound 3.10, was discovered to be less hazardous to normal and pseudonormal cells while still having cytotoxic effects comparable to those of doxorubicin (IC50 varied from 0.6 to 5.98 M). Although the strength of the interactions between all synthesised chemicals and DNA did not correspond with their anticancer effect, they could all interact with DNA. P53 status in colorectal cancer. [40]

## 3. Conclusion

The commercially utilized medications no longer have any of the 4-thiazolidinone nucleus' efficacy. Although the four principal classes of drugs are antibacterial, antitubercular, antiviral, and diabetic (PTP1B inhibitors), Other possible targets and areas of therapeutic

usage need to be investigated. The majority of locations were investigated to enhance the 4-thiazolidinone's antibacterial and antitubercular profile, however none of the derivatives shown encouraging antitubercular activity. However, only a small number of derivatives with C-2 and N-3 substituted positions and the presence of an electron-withdrawing substitution on the aromatic ring in the C-2 position of 4-thiazolinone present varying degrees of inhibition against Gram-positive and Gram-negative bacteria, demonstrating inhibition that is as effective as that of the commonly used standard medications.

**Reference:**

1. Deng JC. Viral–bacterial interactions–therapeutic implications. Influenza and other respiratory viruses. 2013 Nov; 7:24-35.
2. Gouveia FL, de Oliveira RM, de Oliveira TB, da Silva IM, do Nascimento SC, de Sena KX, de Albuquerque JF. Synthesis, antimicrobial and cytotoxic activities of some 5-arylidene-4-thioxo-thiazolidine-2-ones. European journal of medicinal chemistry. 2009 May 1;44(5):2038-43.
3. Tariq S, Wani S, Rasool W, Shafi K, Bhat MA, Prabhakar A, Shalla AH, Rather MA. A comprehensive review of the antibacterial, antifungal and antiviral potential of essential oils and their chemical constituents against drug-resistant microbial pathogens. Microbial pathogenesis. 2019 Sep 1;134:103580.
4. Sahiba N, Sethiya A, Soni J, Agarwal DK, Agarwal S. Saturated five-membered thiazolidines and their derivatives: from synthesis to biological applications. Topics in Current Chemistry. 2020 Apr;378(2):34.
5. Pathania S, Narang RK, Rawal RK. Role of sulphur-heterocycles in medicinal chemistry: An update. European journal of medicinal chemistry. 2019 Oct 15;180:486-508.Tomasic T, Masic LP. Rhodanine as a privileged scaffold in drug discovery. Current Medicinal Chemistry. 2009 May 1;16(13):1596-629.
6. Sainsbury M. Five-Membered Heterocyclic Compounds with Two Different Hetero-Atoms in the Ring. InRodd's Chemistry of Carbon Compounds 1964 Jan 1 (pp. 243-504). Elsevier.
7. BROWN FC, BRADSHER CK, MOSER BF, FORRESTER S. Structure and antimicrobial activity of the 3-aminorhodanines. The Journal of Organic Chemistry. 1959 Aug;24(8):1056-60.
8. Tripathi AC, Gupta SJ, Fatima GN, Sonar PK, Verma A, Saraf SK. 4-Thiazolidinones: the advances continue…. European Journal of Medicinal Chemistry. 2014 Jan 24;72:52-77.
9. NAGASE H. Studies on Fungicides. XXI. Reaction of Dimethyl Acetylenedicarboxylate with Thioureas. Chemical and Pharmaceutical Bulletin. 1973 Feb 25;21(2):270-8.
10. Ibrahim AM, Shoman ME, Mohamed MF, Hayallah AM, Abuo-Rahma GE. Chemistry and Applications of Functionalized 2, 4- Thiazolidinediones. European Journal of Organic Chemistry.:e202300184.
11. Lesyk RB, Zimenkovsky BS, Kaminskyy DV, Kryshchyshyn AP, Havryluk RB, Atamanyuk DV, Subtel'na IY, Khyluk DV. Thiazolidinone motif in anticancer drug discovery. Experience of DH LNMU medicinal chemistry scientific group. Biopolymers and Cell. 2011.

12. Verma A, Saraf SK. 4-Thiazolidinone–A biologically active scaffold. European journal of medicinal chemistry. 2008 May 1;43(5):897-905.
13. Jain VS, Vora DK, Ramaa CS. Thiazolidine-2, 4-diones: Progress towards multifarious applications. Bioorganic & medicinal chemistry. 2013 Apr 1;21(7):1599-620.
14. Metwally MA, Farahat AA, Abdel-Wahab BF. 2-Amino-4-thiazolidinones: synthesis and reactions. Journal of Sulfur Chemistry. 2010 Aug 1;31(4):315-49.
15. Jain AK, Vaidya A, Ravichandran V, Kashaw SK, Agrawal RK. Recent developments and biological activities of thiazolidinone derivatives: A review. Bioorganic & medicinal chemistry. 2012 Jun 1;20(11):3378-95.
16. Singh SP, Parmar SS, Raman K, Stenberg VI. Chemistry and biological activity of thiazolidinones. Chemical Reviews. 1981 Apr 1;81(2):175-203.
17. Ali M, Soliman F, Mohramb ME. Synthesis, Molecular Docking and Antimicrobial Activities of 3-Formyl-2-(1H) quinolinone Schiff Base Derivatives and 3-(((3-Acetylphenyl) imino)-methyl) quinolin-2-(1H)-one Chalcone Derivatives. Egyptian Journal of Chemistry. 2020 Oct 1;63(10):3903-14.
18. Khajeh-Amiri A, Foroughifar N, Hassannejad F, Esfahani B, Zanganeh A. Microwave assisted highly efficient synthesis of rhodanine and-2, 4-thiazolidinedione derivatives under solvent free conditions. Current Microwave Chemistry. 2018 Sep 1;5(3):215-24.
19. Shahin Azad, M., 2017. Synthesis of thiazolidinone derivatives containing thiadiazoline moiety of biological interest.
20. Archna, Chawla PA, Teli G, Pathania S, Singh S, Srivastava V. Exploration of Antioxidant, Anti-inflammatory and Anticancer Potential of Substituted 4-Thiazolidinone Derivatives: Synthesis, Biological Evaluation and Docking Studies. Polycyclic Aromatic Compounds. 2023 Jan 2;43(1):597-618.
21. Ahmadi M, Bekeschus S, Weltmann KD, von Woedtke T, Wende K. Non-steroidal anti-inflammatory drugs: recent advances in the use of synthetic COX-2 inhibitors. RSC Medicinal Chemistry. 2022.
22. Haroun M, Petrou A, Tratrat C, Kositsi K, Gavalas A, Geronikaki A, Venugopala KN, Sreeharsha N. Discovery of benzothiazole-based thiazolidinones as potential anti-inflammatory agents: Anti-inflammatory activity, soybean lipoxygenase inhibition effect and molecular docking studies. SAR and QSAR in Environmental Research. 2022 Jun 3;33(6):485-97.
23. Desai NC, Jadeja DJ, Jethawa AM, Ahmad I, Patel H, Dave BP. Design and synthesis of some novel hybrid molecules based on 4-thiazolidinone bearing pyridine-pyrazole scaffolds: molecular docking and molecular dynamics simulations of its major constituent onto DNA gyrase inhibition. Molecular Diversity. 2023 Feb 8:1-7.
24. Haroun, M., Petrou, A., Tratrat, C., Kositsi, K., Gavalas, A., Geronikaki, A., Venugopala, K.N. and Sreeharsha, N., 2022. Discovery of benzothiazole-based thiazolidinones as potential anti-inflammatory agents: Anti-inflammatory activity, soybean lipoxygenase inhibition effect and molecular docking studies. *SAR and QSAR in Environmental Research*, *33*(6), pp.485-497.
25. Haroun, Michelyne, AnthiPetrou, Christophe Tratrat, AggelikiKolokotroni, Maria Fesatidou, Panagiotis Zagaliotis, Antonis Gavalas, Katharigatta N. Venugopala, NagarajaSreeharsha, Anroop B. Nair, Heba SadekElsewedy, and AthinaGeronikaki. 2022.

"Discovery of 5-Methylthiazole-Thiazolidinone Conjugates as Potential Anti-Inflammatory Agents: Molecular Target Identification and In Silico Studies" *Molecules* 27, no. 23: 8137. https://doi.org/10.3390/molecules27238137

**26.** Karapetyan LV, Tokmajyan GG. Catalyst- Free Synthesis of New Iminodihydrofurans Containing Thiazolidinone Ring. ChemistrySelect. 2022 Nov 25;7(44):e202202745..

27. Abd El-Karim SS, Mohamed HS, Abdelhameed MF, Amr AE, Almehizia AA, Nossier ES. Design, synthesis and molecular docking of new pyrazole-thiazolidinones as potent anti-inflammatory and analgesic agents with TNF-α inhibitory activity. Bioorganic chemistry. 2021 Jun 1;111:104827.
28. Adnan AM, Mahdi MF, kareem Khan A. Design, Synthesis, and Acute Anti-inflammatory Assessment of New 2-methyl Benzoimidazole Derivatives Having 4-Thiazolidinone Nucleus. Al Mustansiriyah Journal of Pharmaceutical Sciences. 2019 Dec 1;19(4):151-60.
29. Abdellatif KR, Fadaly WA, Kamel GM, Elshaier YA, El-Magd MA. Design, synthesis, modeling studies and biological evaluation of thiazolidine derivatives containing pyrazole core as potential anti-diabetic PPAR-γ agonists and anti-inflammatory COX-2 selective inhibitors. Bioorganic chemistry. 2019 Feb 1;82:86-99.
30. SHAWKY, Ahmed M., et al. Optimization of pyrrolizine-based Schiff bases with 4-thiazolidinone motif: Design, synthesis and investigation of cytotoxicity and anti-inflammatory potency. *European journal of medicinal chemistry*, 2020, 185: 111780.
31. Omar YM, Abdu-Allah HH, Abdel-Moty SG. Synthesis, biological evaluation and docking study of 1, 3, 4-thiadiazole-thiazolidinone hybrids as anti-inflammatory agents with dual inhibition of COX-2 and 15-LOX. Bioorganic chemistry. 2018 Oct 1;80:461-71.
32. Liaras K, Fesatidou M, Geronikaki A. Thiazoles and thiazolidinones as COX/LOX inhibitors. Molecules. 2018 Mar 18;23(3):685.
33. Manju SL, Ethiraj KR, Elias G. Safer anti-inflammatory therapy through dual COX-2/5-LOX inhibitors: A structure-based approach. European Journal of Pharmaceutical Sciences. 2018 Aug 30;121:356-81.
34. Ottanà R, Paoli P, Naß A, Lori G, Cardile V, Adornato I, Rotondo A, Graziano AC, Wolber G, Maccari R. Discovery of 4-[(5-arylidene-4-oxothiazolidin-3-yl) methyl] benzoic acid derivatives active as novel potent allosteric inhibitors of protein tyrosine phosphatase 1B: In silico studies and in vitro evaluation as insulinomimetic and anti-inflammatory agents. European Journal of Medicinal Chemistry. 2017 Feb 15;127:840-58.
35. Akhtar J, Khan AA, Ali Z, Haider R, Yar MS. Structure-activity relationship (SAR) study and design strategies of nitrogen-containing heterocyclic moieties for their anticancer activities. European journal of medicinal chemistry. 2017 Jan 5;125:143-89.
36. Kumar A, Rajput CS, Bhati SK. Synthesis of 3-[4′-(p-chlorophenyl)-thiazol-2′-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethyl]-6-bromoquinazolin-4-ones as anti-inflammatory agent. Bioorganic & medicinal chemistry. 2007 Apr 15;15(8):3089-96.
37. Amin KM, Kamel MM, Anwar MM, Khedr M, Syam YM. Synthesis, biological evaluation and molecular docking of novel series of spiro [(2H, 3H) quinazoline-2, 1′-

cyclohexan]-4 (1H)-one derivatives as anti-inflammatory and analgesic agents. European Journal of Medicinal Chemistry. 2010 Jun 1;45(6):2117-31.

38. Vigorita MG, Ottana R, Monforte F, Maccari R, Trovato A, Monforte MT, Taviano MF. Synthesis and antiinflammatory, analgesic activity of 3, 3′-(1, 2-Ethanediyl)-bis [2-aryl-4-thiazolidinone] chiral compounds. Part 10. Bioorganic & Medicinal Chemistry Letters. 2001 Nov 5;11(21):2791-4.
39. Gornowicz A, Lesyk R, Czarnomysy R, Holota S, Shepeta Y, Popławska B, Podolak M, Szymanowski W, Bielawski K, Bielawska A. Multi-Targeting Anticancer Activity of a New 4-Thiazolidinone Derivative with Anti-HER2 Antibodies in Human AGS Gastric Cancer Cells. International Journal of Molecular Sciences. 2023 Apr 5;24(7):6791.
40. Ivasechko I, Lozynskyi A, Senkiv J, Roszczenko P, Kozak Y, Finiuk N, Klyuchivska O, Kashchak N, Manko N, Maslyak Z, Lesyk D. Molecular design, synthesis and anticancer activity of new thiopyrano [2, 3-d] thiazoles based on 5-hydroxy-1, 4-naphthoquinone (juglone). European journal of medicinal chemistry. 2023 Apr 5;252:115304.