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# Exploration of synthetic strategies and therapeutic potential of 4-Thiazolidinones: Current progression and structure activity relationship studies

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**ABSTRACT**
**Thiazolidinone derivatives have divergent and remarkable medicative effect like antioxidant, antimicrobial, anti-inflammatory, anticancer, antidiabetic, anticonvulsant, anti-HIV, antitubercular, antiviral, antimalarial and many more so they are the subject of scientific expedition. 4-Thiazolidinones represent a versatile class of heterocyclic compounds that have attracted significant attention due to their broad spectrum of biological activities and synthetic adaptability. Over the past decades, diverse synthetic strategies have been developed to access 4-thiazolidinone scaffolds, including cyclization of thiosemicarbazones, condensation reactions with α-halo acids, and multicomponent approaches that enable structural diversity. These methodologies not only streamline synthesis but also facilitate the incorporation of pharmacophoric groups, enhancing drug-like properties. Current progression in medicinal chemistry highlights the therapeutic potential of 4-thiazolidinones across multiple domains, such as antimicrobial, anticancer, anti-inflammatory, antiviral, and antidiabetic applications. Structure–activity relationship (SAR) studies reveal that substitution at the C-2 and C-5 positions of the thiazolidinone ring plays a pivotal role in modulating biological activity, with electron-withdrawing groups often improving potency. Furthermore, hybrid molecules combining 4-thiazolidinone cores with other pharmacophores have demonstrated synergistic effects, underscoring their promise in rational drug design. Despite encouraging preclinical findings, challenges remain in optimizing pharmacokinetics and minimizing toxicity, necessitating further exploration of analog libraries and computational modeling. Overall, the integration of innovative synthetic strategies with SAR-guided design continues to expand the therapeutic landscape of 4-thiazolidinones, positioning them as valuable candidates in modern drug discovery pipelines. The present study offers an in-depth review of current progression (2014–2025) in the biological activities and structure–activity relationship (SAR) of derivatives of 4-thiazolidinone through systematic literature survey.**



## 1. INTRODUCTION:

Heterocyclic composites, a substantial class of organic molecules with an extensive array of uses in scientific domain [1]. Data signify that near 85% of all physiologically active chemical entities comprises heterocycles. This highlights the prominence of heterocycles in current medication development [2]. Optimization of the ADME characteristics of drug candidate can be achieved by the use of heterocycles which modify the

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lipophilicity, solubility, polarity and hydrogen bonding capacity of biologically active compounds [3]. Among a wide class of heterocycles, nitrogen containing heterocycles are the most significant one which are abundant in physiologically active structures, medicinal compound and naturally occurring compounds [4]. The most well-known of this is thiazolidinone, which has a carbonyl group at 2, 4, or 5-position, a nitrogen atom at 3-position, and a sulfur atom at 1-position. It has drawn a lot of attention over the years due to its importance and versatility in the field of Medicinal Chemistry [5]. For the designing of new compounds thiazolidinone is unceasingly being used. Thiazolidinone has emerged as one of the most potent and substantial heterocyclic compounds owing to its numerous physiological responses [6]. A large number of substituents are feasible at position 2, 4 and 5 of thiazolidinone nucleus which shoot up its medicinal significance (Figure 1) [8].Thiazolidine and its derivatives are indispensable component in a large number of pharmaceuticals, naturally available products and diverse chemical entities for instance anticancer, antimicrobial, antidiabetic, anti-inflammatory, antitubercular, antifungal, antiviral, antiHIV, cytotoxicity, antitrypanosomal, anticonvulsant, antioxidant, antinociceptive and anti-hypernociceptive compounds, antialzheimer's, antimalarial and various other pharmacological activites [9-12].

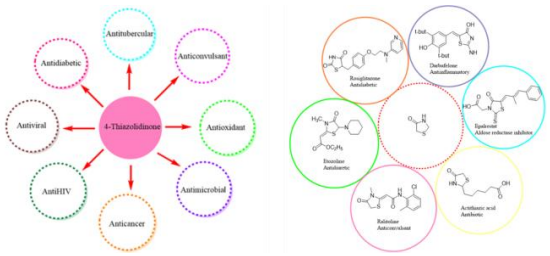


**Figure 1: Therapeutic Potential of 4-thiazolidinone Scaffold**

## 2. Structure Related Aspects

Various isomers of thiazolidinones are depicted in figure 2 with nomenclature [13]. The 4-thiazolidinone nucleus is found in several compounds with a variety of biological functions [14].

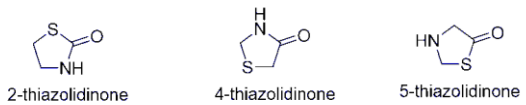


**Figure 2: Various isomers of Thiazolidinones**

From the various literature studies, it was found that the pseudo-thiohydantoin's and rhodamine's noncyclic structure was initially suggested due to the confusion regarding the structure of thiazolidin-4-ones [15]. The carbon atom of methylene at position 5 in analogs of thiazolidin-4-one exhibits nucleophilic activity, and several pursuits have been made to perform the Knoevenagel reaction of this methylene group [16]. To establish a pertinence amid the biological functions and basicity of thiazolidin-4-ones, it is pivotal to apprehend their structural and conformational characteristics. An array of configurations discovered having similarity with envelope or half-chair shape, along with other optical, geometrical, and regioselective isomers of thiazolidin-4-one derivatives that have been proclaimed [17].

## 3. Characteristics Properties of Thiazolidinones:

### 3.1 Physical Characteristics:

Substitution at position 3 of 4-thiazolidinone results in a solid compound which melts with decomposition. Alkyl substitution at the nitrogen atom decreases their melting point. Thiazolidinones that are not substituted with aryl or higher alkyl substituents exhibits some degree of solubility in water [18].

### 3.2 Chemical Characteristics:

4-Thiazolidinones are five-membered heterocyclic compounds characterized by a thiazolidine ring with a carbonyl group at the 4-position, giving them unique electronic, structural, and pharmacological properties. Their chemical versatility arises from substitution at the C-2 and C-5 positions, which strongly influences biological activity and synthetic utility [19, 20]. 4-Thiazolidinones are a distinctive class of heterocyclic compounds characterized by a five-membered thiazolidine ring containing both sulfur and nitrogen atoms, with a carbonyl group located at the 4-position. This structural arrangement imparts unique electronic and physicochemical properties that make the scaffold highly versatile in medicinal chemistry [21, 22]. The presence of heteroatoms within the ring contributes to polarity, hydrogen-bonding potential, and reactivity, while the carbonyl group enhances electrophilicity and provides a site for tautomerism and resonance stabilization [23, 24]. The most chemically significant positions on the ring are C-2 and C-5, which are highly amenable to substitution. Modifications at these sites allow fine-tuning of lipophilicity, polarity, and electronic distribution, thereby influencing biological activity and pharmacokinetic behavior [25]. For instance, aryl or heteroaryl substitution at C-2 often enhances antimicrobial and anticancer potency, while electron-withdrawing groups at C-5 improve anti-inflammatory and enzyme inhibitory activity. The scaffold also exhibits keto–enol tautomerism, which can alter binding interactions with biological targets depending on solvent polarity and substituent effects [26, 27].

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From a synthetic perspective, 4-thiazolidinones are readily accessible through cyclization reactions involving thiosemicarbazones and α-halo acids, as well as multicomponent reactions that enable rapid diversification of analog libraries [28, 29]. Their chemical stability under physiological conditions, combined with moderate polarity, makes them suitable for drug design, while their reactivity allows incorporation of diverse pharmacophores to generate hybrid molecules with synergistic activity [30]. Physicochemically, 4-thiazolidinones display tunable lipophilicity, which influences membrane permeability and bioavailability, and their moderate solubility in polar solvents facilitates formulation. The sulfur atom contributes to unique electronic effects, often enhancing binding affinity to enzyme active sites or receptor pockets [31, 32].

Additionally, the scaffold's ability to engage in hydrogen bonding and π–π stacking interactions broadens its pharmacological relevance. Overall, the chemical characteristics of 4-thiazolidinones—structural flexibility, electronic adaptability, and synthetic accessibility—make them a privileged scaffold in medicinal chemistry. Their capacity for structural modification at key positions, combined with favorable physicochemical traits, underpins their wide-ranging biological activities, including antimicrobial, anticancer, anti-inflammatory, antiviral, and antidiabetic effects [33, 34]. Continued exploration of their chemical properties through structure–activity relationship studies (Figure 3) and computational modeling is expected to further enhance their therapeutic potential and establish them as valuable candidates in modern drug discovery pipelines [35-39].

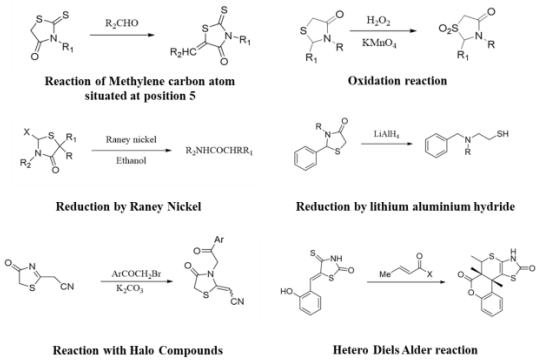



**Figure 3: Structure–Activity Relationship Studies**

## 4. Synthesis of 4-thiazolidinones:

4-Thiazolidinones are typically prepared via a three-component cyclocondensation of a primary amine (or amino acid), an aldehyde, and mercaptoacetic (thioglycolic) acid. The amine and aldehyde first form an imine (Schiff base), which undergoes nucleophilic addition by the thiol, followed by intramolecular acylation to close the five-membered ring and install the 4-oxo function. Variants include using isothiocyanates or carbon disulfide to generate thioimidates that cyclize with chloroacetic acid, and Knoevenagel–Michael sequences where activated methylene compounds (e.g., malononitrile) form adducts that trap thiols before ring closure. Lewis acids ($ZnCl_2$, $BF_3 \cdot Et_2O$), Brønsted acids (p-TsOH, AcOH), bases (piperidine), or ionic liquids can accelerate imine formation and cyclization; microwave irradiation often shortens reaction times from hours to minutes. For N- or C-substitution, prefunctionalized amines/aldehydes or post-cyclization modifications (halogenation, alkylation, acylation) are used. Asymmetric approaches employ chiral amines or organocatalysts to induce enantioselectivity. Green adaptations leverage water, glycerol, deep eutectic solvents, or solid acids, minimizing waste and purification steps. Overall, multicomponent strategies provide efficient, modular access to diverse 4-thiazolidinone libraries (Figure 4).

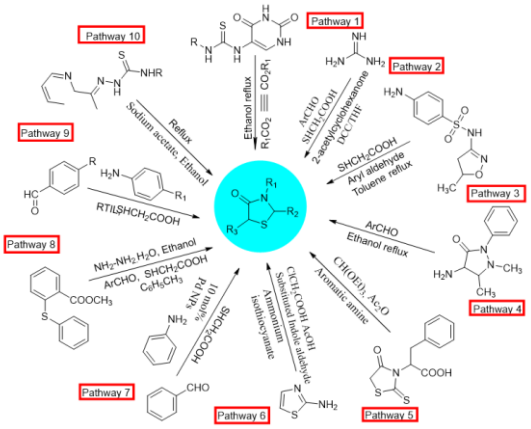
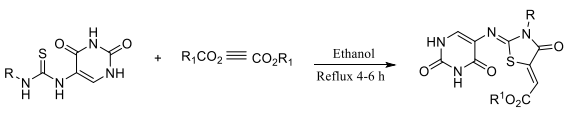



**Figure 4: Various synthetic routes for the synthesis of 4-thiazolidinone derivatives**

**4.1 Synthetic route 1**, Alshammari and coworkers, developed a unique category of pyrimidine-containing thiazolidinone compounds. The approach involved refluxing substituted thioureas with acetylenedicarboxylate derivatives in methanol for 4–6 hours, yielding substituted thiazolidinones in 76–85% yield. Spectral and elemental analysis confirmed the successful synthesis of these compounds [40, 41].




**4.2 Synthetic route 2**, Amit *et al.,* developed new 4-thiazolidinone derivatives using a two-step process. First, guanidine reacted with 1,3-dicarbonyl compounds to form intermediate 2-aminopyrimidine derivatives. Then, these intermediates were cyclized with DCC and treated with mercaptoacetic acid and aryl aldehyde to

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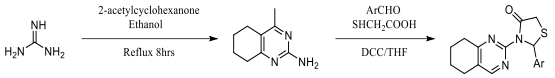
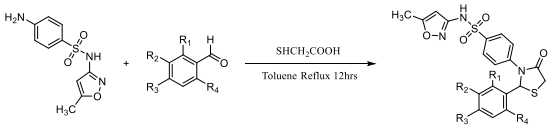
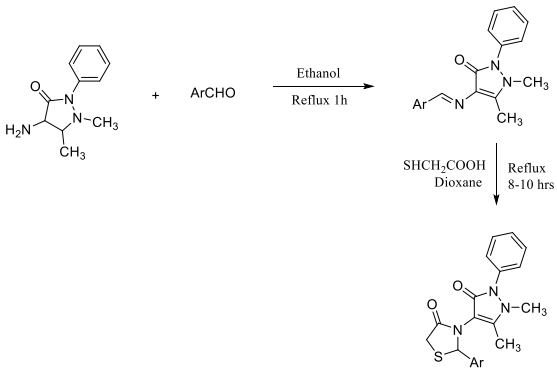
create final compounds [42, 43].



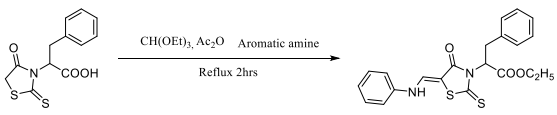

**4.3 synthetic route 3,** Bhat and his colleagues, developed sulfamethoxazole-based 4-thiazolidinone hybrid through a cyclocondensation reaction. This process involved reacting substituted benzenesulfonamide, an aromatic aldehyde, and $SHCH_2COOH$, yielding the desired products in good to excellent yields [44, 45].



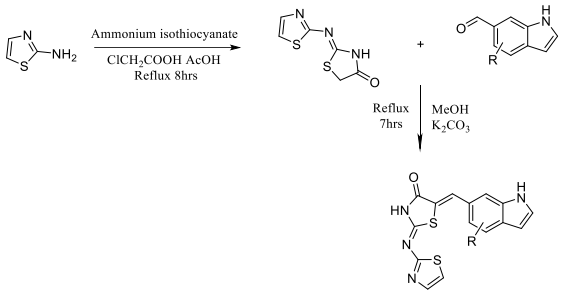

**4.4 synthetic route 4**, Rahman *et al.,* developed novel 4-thiazolidinones incorporating an antipyrine moiety. Schiff's bases were produced by condensing 4-aminoantipyrine with a halogenated aromatic aldehyde in refluxing ethanol. In this path, mercaptoacetic acid was refluxed with Schiff's base using non-polar solvent dioxane to create substituted 4-thiazolidinones [46, 47].



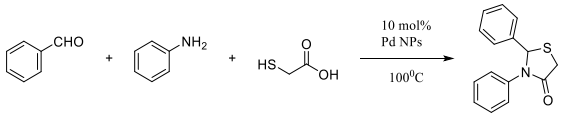

**4.5 synthetic route 5**, a new series of 5-enamine-4-thiazolidinones was designed by Holota *et al.,* In this innovative approach, 2-(4-oxo-2-thioxothiazolidin-3-yl)-3-phenylpropionic acid was reacted with triethyl orthoformate in acetic anhydride medium. Furthermore, this resultant intermediate was refluxed in ethanol medium with the appropriate amine for 2 hours to yield targeted compound 2-(5-R-aminomethylene-4- oxo-2-thioxothiazolidin-3-yl)-3-phenylpropionic acid ethyl esters. After filtering out the resulting solid products, they were cleaned with ethanol and recrystallized from either ethanol or a 1:1 ethanol:water combination [48].



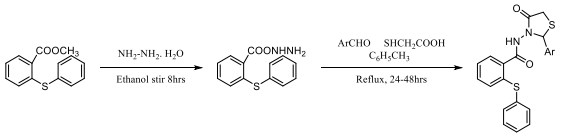

**4.6 synthetic route 6**, a novel series of indole fused thiazolidinones was created by Khan *et al.,* This approach produced thiazole-bearing thiourea by refluxing 2-aminothiazole and ammonium isothiocyanate for four hours. This intermediate produced a thiazole-based thiazolidinone moiety after additional refluxing with chloroacetic acid in an acidified solution employing acetic acid for around five hours. Thiazolidinone-based indole analogues were produced by reacting substituted indole-bearing aldehydes with the aforementioned intermediate in the presence of potassium carbonate [49].




**4.7 synthetic route 7**, Harale *et al.,* prepared 2,3-diaryl-4-thiazolidinones. This method involved the catalytic reaction of 10 mol% Pd NPs with aromatic amine, aromatic aldehyde, and mercaptoacetic acid, followed by agitation at $100^0$C. Thin layer chromatography employed for the monitering of the reaction using a mixture of ethyl acetate: n-hexane (3:7) [50].




**4.8 synthetic route 8**, Tahmasvand et al created a sequence of novel derivatives by stirring methyl-2-(phenylthio) benzoate with hydrazine hydrate in ethanol to give the intermediate hydrazide. The hydrazide was refluxed with aromatic aldehyde, thioglycolic acid in toluene to give the final product diphenyl thioether fused thiazolidinones [51]




**4.9 synthetic route 9**, a feasible novel procedure for thiazole-clubbed with thiazolidinones was created by Khilare *et al.* This synthesis method produced a 4-thiazolidinone nucleus-containing product by reacting aromatic amines, mercapto acetic acid and aromatic carbaldehyde, and in di-isopropyl ethyl ammonium acetate at ambient temperature [52].

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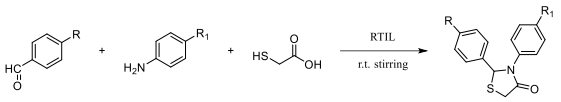
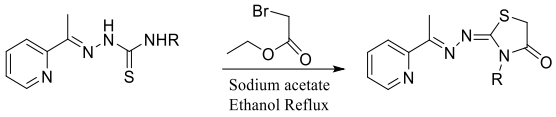



**4.10 synthetic route 10**, Kassem et al designed and synthesized pyridine conjugated thiazolidinone derivatives. This technique produced a 90% yield by refluxing for 8 hours with thiosemicarbazone derivative, ethyl bromoacetate, anhydrous sodium acetate and absolute ethanol. The solid product was purified with water and recrystallized from 100% ethanol, and the reaction's progress was tracked using TLC [53].




## 5. Pharmacological Importance of Thiazolidinones and its derivatives

The pharmacological effects of thiazolidinones are mediated through various mechanisms depending on the specific derivative and target disease. Many thiazolidinones act by inhibiting key enzymes or interacting with cellular receptors [54]. For instance, some derivatives inhibit bacterial DNA gyrase or topoisomerase, leading to antimicrobial effects. Others modulate peroxisome proliferator-activated receptors (PPARs), particularly PPARγ, which plays a crucial role in glucose metabolism and insulin sensitivity. Additionally, thiazolidinones can induce apoptosis in cancer cells by activating caspases or disrupting mitochondrial function [55].

### 5.1 Anti-Oxidant Activity:

Thiazolidinone derivatives have attracted considerable attention for their antioxidant activity, which plays a crucial role in combating oxidative stress–related disorders such as cancer, diabetes, neurodegeneration, and cardiovascular diseases [56]. These compounds act primarily by scavenging free radicals like DPPH and ABTS, donating hydrogen atoms or electrons to neutralize reactive oxygen species (Figure 5).

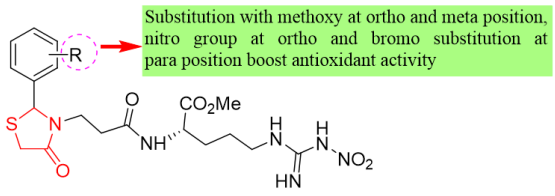



**Figure 5: Anti-Oxidant Activity**

In addition, certain thiazolidinones exhibit metal-chelating properties, reducing the catalytic activity of transition metals that drive oxidative damage (57). Structural modifications, particularly the incorporation of electron-donating substituents such as hydroxyl or methoxy groups, significantly enhance their radical scavenging potential. Studies have shown that some thiazolidinone derivatives demonstrate $IC_{50}$ values comparable to ascorbic acid, underscoring their potency as antioxidant agents [58]. By preventing lipid peroxidation and stabilizing cellular membranes, these molecules not only protect against oxidative injury but also complement their other pharmacological effects, including anti-inflammatory and anticancer activities. Thus, thiazolidinones represent a promising scaffold for the development of multifunctional drugs aimed at managing diseases linked to oxidative stress [59].

### 5.2 Anti Inflammatory Activity:

Thiazolidinone derivatives exhibit notable anti-inflammatory activity, making them promising candidates for managing conditions associated with excessive inflammation. Their mechanism of action often involves the inhibition of cyclooxygenase (COX) enzymes, which reduces the synthesis of pro-inflammatory prostaglandins [60]. In addition, many thiazolidinones suppress the release of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, thereby modulating the immune response [61]. Some derivatives also interfere with NF-κB signaling pathways, a key regulator of inflammation, leading to decreased expression of inflammatory mediators (Figure 6).

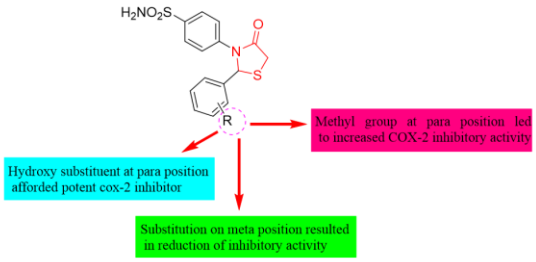



**Figure 6: Anti Inflammatory Activity**

Structural modifications, particularly the introduction of electron-donating or halogen substituents, have been shown to enhance anti-inflammatory potency [62]. Experimental studies using animal models of inflammation, such as carrageenan-induced paw edema, have confirmed the efficacy of thiazolidinones in reducing swelling and pain. By combining anti-inflammatory effects with other pharmacological properties (antioxidant, analgesic, anticancer), thiazolidinones represent a versatile scaffold for the development of multifunctional therapeutic agents aimed at treating chronic inflammatory diseases [63].

### 5.3 Anti-Microbial Activity:

Thiazolidinone derivatives display remarkable anti-microbial activity, making them valuable scaffolds

in the development of new therapeutic agents against resistant pathogens. Their effectiveness has been demonstrated against a wide range of Gram-positive and Gram-negative bacteria, as well as various fungal strains [64]. The mechanism of action often involves inhibition of bacterial enzymes such as DNA gyrase and topoisomerase, disruption of cell wall synthesis, or interference with nucleic acid replication, ultimately leading to microbial cell death [65]. Structural modifications (Figure 7), particularly the incorporation of halogen atoms, nitro groups, or aromatic substituents, have been shown to significantly enhance antimicrobial potency. In addition, thiazolidinones can act synergistically with existing antibiotics, offering potential solutions to combat multi-drug resistant organisms. Their antifungal activity is attributed to the inhibition of ergosterol biosynthesis and disruption of fungal membrane integrity. Because of their broad spectrum and adaptability, thiazolidinones are considered promising candidates for the design of next-generation antimicrobial agents, addressing the urgent need for effective drugs in the face of rising antimicrobial resistance [66, 67].

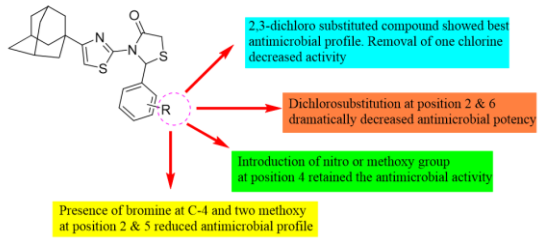



**Figure 7: Anti-Microbial Activity**

### 5.4 Anti Cancerous Activity:

Thiazolidinone derivatives have shown promising anti-cancerous activity, positioning them as potential scaffolds for novel anticancer drug development. Their mechanisms of action are diverse, including the induction of apoptosis through activation of caspases and disruption of mitochondrial membrane potential, as well as cell cycle arrest at various checkpoints to inhibit uncontrolled proliferation [68]. Structural modifications (Figure 8), particularly the incorporation of aromatic or heteroaromatic substituents, have been found to enhance cytotoxicity against a wide range of cancer cell lines, including breast, lung, colon, and leukemia [69].

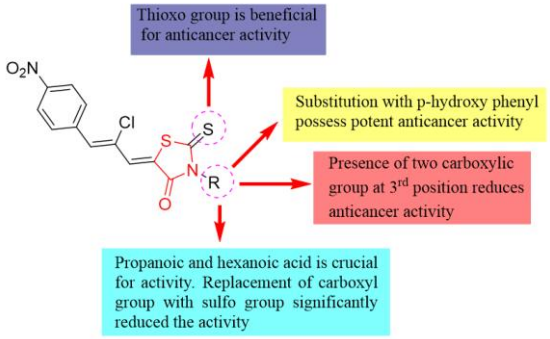



**Figure 8: Anti Cancerous Activity**

Some derivatives interfere with angiogenesis, thereby preventing tumor growth and metastasis, while others inhibit key enzymes and signaling pathways such as tyrosine kinases and NF-κB that are critical for cancer cell survival [70]. Importantly, thiazolidinones often exhibit selectivity toward malignant cells with reduced toxicity to normal tissues, making them attractive candidates for safer chemotherapy. Their ability to combine anticancer effects with other pharmacological properties, such as antioxidant and anti-inflammatory activities, further strengthens their therapeutic potential in the multifaceted management of cancer [71, 72].

### 5.5 Anticonvulsant Activity:

Thiazolidinone derivatives have been widely investigated for their anticonvulsant activity, showing promising results in experimental models of epilepsy. These compounds exert their effects primarily by modulating neurotransmitter systems and stabilizing neuronal excitability [73]. Some derivatives act through enhancement of GABAergic transmission, thereby increasing inhibitory signaling in the central nervous system, while others inhibit voltage-gated sodium and calcium channels, reducing excessive neuronal firing that leads to seizures. Structural modifications (Figure 9), such as the introduction of aromatic substituents or halogen groups, have been found to significantly improve anticonvulsant potency. In animal studies, thiazolidinones have demonstrated protection against chemically induced seizures (e.g., pentylenetetrazole and maximal electroshock models), highlighting their potential as effective agents for seizure management [74, 75].

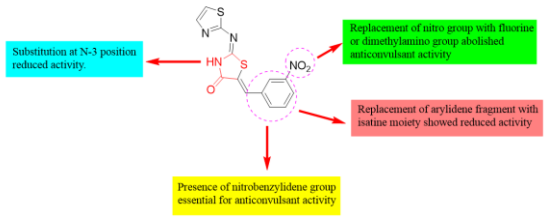



**Figure 9: Anticonvulsant Activity**

### 5.6 Antidiabetic Activity

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Thiazolidinone derivatives have been extensively studied for their antidiabetic activity, particularly in the management of type 2 diabetes mellitus. Their primary mechanism involves activation of peroxisome proliferator-activated receptor gamma (PPARγ), a nuclear receptor that regulates glucose and lipid metabolism [76]. By acting as PPARγ agonists, thiazolidinones enhance insulin sensitivity, promote glucose uptake in peripheral tissues, and improve overall glycemic control. In addition, some derivatives reduce hepatic glucose production and modulate adipocyte differentiation, contributing to better metabolic balance. Structural modifications (Figure 10), such as substitution at the 2- or 5-position of the thiazolidinone ring, have been shown to improve potency and selectivity, while minimizing adverse effects associated with earlier drugs like rosiglitazone and pioglitazone [77].

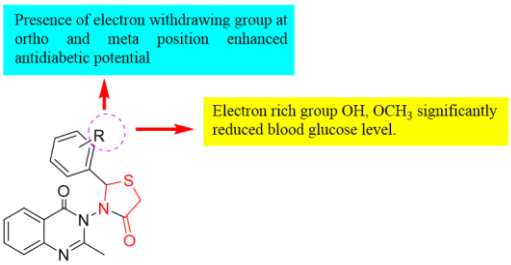


**Figure 10: Antidiabetic Activity**

Beyond glycemic regulation, certain thiazolidinones also exhibit anti-inflammatory and antioxidant properties, which further support their role in mitigating complications of diabetes, including cardiovascular and renal disorders. Thus, thiazolidinones represent a versatile scaffold for the development of next-generation antidiabetic agents with improved safety and efficacy profiles [78, 79].

### 5.7 Anti-Malarial Activity:

Thiazolidinone derivatives have been explored for their antimalarial activity, showing potential against Plasmodium species, the causative agents of malaria. Their mechanism of action often involves inhibition of parasite enzymes essential for survival, such as cysteine proteases and dihydrofolate reductase, which disrupt protein processing and nucleic acid synthesis within the parasite [80, 81]. Some derivatives also interfere with heme detoxification pathways, leading to accumulation of toxic free heme in the parasite's digestive vacuole. Structural modifications (Figure 11), particularly the incorporation of aromatic substituents and electron-donating groups, have been reported to enhance antimalarial potency [82]. In experimental studies, thiazolidinones demonstrated significant activity against both chloroquine-sensitive and chloroquine-resistant strains of Plasmodium falciparum, highlighting their potential in overcoming drug resistance. Their relatively simple synthesis and structural flexibility make them attractive scaffolds for designing new antimalarial agents. By combining antimalarial effects with other pharmacological properties such as antioxidant and anti-inflammatory activities, thiazolidinones offer promise as multifunctional therapeutic candidates in the ongoing fight against malaria [83, 84].

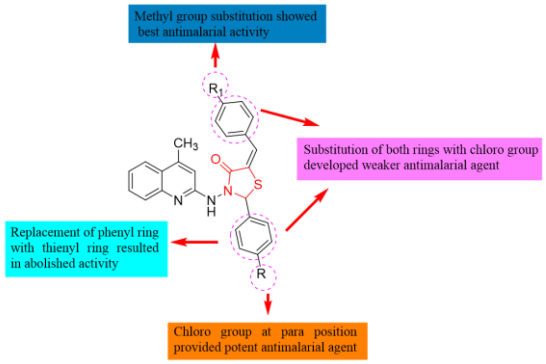


**Figure 11: Anti-Malarial Activity**

### 5.8 Anti-Viral Activity:

Thiazolidinone derivatives have demonstrated noteworthy antiviral activity, making them attractive scaffolds for the development of new antiviral agents. Their mechanisms of action often involve inhibition of viral enzymes such as reverse transcriptase, protease, and integrase, which are essential for viral replication and maturation [85, 86]. Some derivatives also interfere with viral entry and fusion processes, thereby preventing the virus from infecting host cells. Structural modifications (Figure 12), particularly the incorporation of halogen atoms, aromatic substituents, or electron-donating groups, have been shown to enhance antiviral potency [87].

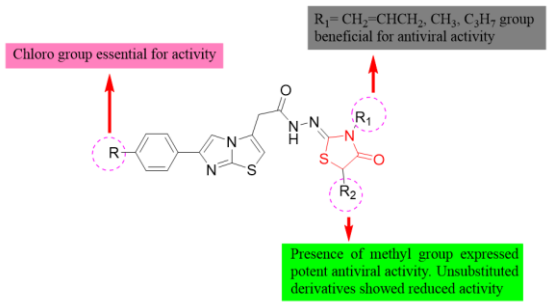


**Figure 12: Anti-Viral Activity**

Experimental studies have reported activity against a variety of viruses, including HIV, hepatitis, influenza, and herpes viruses, highlighting their broad spectrum of efficacy. Importantly, thiazolidinones can act synergistically with existing antiviral drugs, offering potential strategies to overcome drug resistance (88). Their ability to

combine antiviral effects with other pharmacological properties, such as anti-inflammatory and antioxidant activities, further strengthens their therapeutic relevance. Thus, thiazolidinones represent a promising class of compounds for the design of multifunctional antiviral agents aimed at tackling both emerging and resistant viral infections [89, 90].

## 6. CONCLUSIONS:

The exploration of synthetic strategies and therapeutic potential of 4-thiazolidinones underscores their significance as versatile scaffolds in modern medicinal chemistry. Over the years, diverse synthetic methodologies—including multicomponent reactions, cyclocondensation, microwave-assisted synthesis, and green chemistry approaches—have enabled efficient access to structurally varied thiazolidinone derivatives. These strategies not only improve yields and reaction efficiency but also allow fine-tuning of physicochemical properties, thereby expanding the scope of biological applications. The adaptability of the thiazolidinone nucleus has facilitated the incorporation of multiple pharmacophores, resulting in hybrid molecules with enhanced potency and selectivity. From a pharmacological perspective, 4-thiazolidinones exhibit a broad spectrum of activities, including antimicrobial, anticancer, anti-inflammatory, antidiabetic, antiviral, antiparasitic, antioxidant, and anticonvulsant effects. Their ability to interact with diverse biological targets—enzymes, receptors, and signaling pathways—highlights their multifunctional nature. Importantly, structure–activity relationship (SAR) studies have revealed that subtle modifications at the 2, 3, and 5 positions of the thiazolidinone ring can dramatically influence biological activity. For instance, halogen substitutions often enhance antimicrobial potency, while aromatic and heteroaromatic groups improve anticancer efficacy. Such insights provide a rational basis for designing next-generation derivatives with optimized pharmacological profiles. Recent advances, including nanotechnology-based delivery systems, computational modeling, and high-throughput screening, have further accelerated the discovery of novel thiazolidinones with improved pharmacokinetics and reduced toxicity. These innovations strengthen the therapeutic relevance of thiazolidinones, particularly in addressing challenges such as drug resistance and adverse effects associated with conventional therapies. In conclusion, 4-thiazolidinones represent a promising class of heterocycles with immense potential in drug discovery and development. Their synthetic versatility, coupled with diverse pharmacological activities and well-established SAR insights, positions them as valuable candidates for future therapeutic interventions. Continued interdisciplinary research integrating synthetic chemistry, computational tools, and biological evaluation will be pivotal in unlocking the full potential of thiazolidinones as multifunctional therapeutic agents.

**7. Credit authorship contribution statement**
**Anuradha Sharma:** Writing original draft. **Bhawana Sati:** Review and editing **Aakash Deep:** Review and editing. **Arti Soni:** Conceptualization

**8. Ethics approval and consent to participate:** Not applicable.

**9. Consent for publication:** All authors give consent for the publication of the content.

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**14. Abbreviations**

| | |
|---|---|
| NO | Nitric oxide |
| ADME | Absorption, Distribution, Metabolism and Excretion |
| DPPH | Diphenyl picrylhydrazyl |
| COX | Cyclooxygenase |
| TNF | Tumor necrosis factor |
| MIC | Minimum inhibitory concentration |
| MBC | Minimum bactericidal concentration |
| MFC | Minimum fungicidal concentration |
| HER2 | Human epidermal growth factor receptor 2 |
| ROS | Reactive oxygen species |
| LDH | Lactate Dehydrogenase |
| PTZ | Pentylenetetrazole |
| $ED_{50}$ | Median effective dose |
| MES | Maximal electroshock seizure |
| STZ | Streptozotocin |
| G6PD | Glucose-6-phosphate dehydrogenase |

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