Current Chemistry Letters 15 (2026) 627–646

Contents lists available at GrowingScience

Current Chemistry Letters

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Thiazole heterocycles as emerging anti-inflammatory agents: A strategic review

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C H R O N I C L E

Article history:
Received January 5, 2026
Received in revised form
January 27, 2026
Accepted March 27, 2026
Available online
March 27, 2026

Keywords:
Thiazole heterocycles
Anti-Inflammatory agents
COX/LOX inhibition
Prodrug strategies

A B S T R A C T

Thiazole heterocycles have attracted significant attention as versatile scaffolds for the development of novel anti-inflammatory agents. Their structural diversity, ease of functionalization, and ability to interact with multiple molecular targets make them particularly attractive for addressing complex inflammatory pathologies. This review provides a comprehensive and strategic overview of thiazole-based anti-inflammatory compounds, highlighting structural classes, and mechanistic insights. Particular emphasis is placed on multi-target approaches that combine anti-inflammatory and antioxidant properties, as well as the design of prodrug and hybrid molecules aimed at improving pharmacokinetic profiles. Despite promising preclinical data, translational challenges remain, including limited in vivo validation, variability in experimental models, and gaps in ADME/toxicity profiling. We discuss future directions, emphasizing the need for standardized testing protocols, advanced computational design, and integrated medicinal chemistry strategies to accelerate the development of clinically viable thiazole-based anti-inflammatory drugs.

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1. Introduction

Inflammation represents a complex, tightly regulated physiological response that is essential for host defense and tissue repair. However, when the inflammatory process becomes chronic or dysregulated, it contributes to the pathogenesis of a broad range of diseases, including rheumatoid arthritis, inflammatory bowel disease, neurodegenerative disorders, and cancer.[1-3] Despite the substantial therapeutic advances achieved with conventional anti-inflammatory agents such as non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, their long-term use is frequently associated with significant gastrointestinal, cardiovascular, and metabolic adverse effects.[4-6] Consequently, the need for novel anti-inflammatory therapies with enhanced efficacy, improved selectivity, and a superior safety profile remains a major unmet medical challenge.

In this context, thiazole-based heterocycles have emerged as a privileged scaffold in medicinal chemistry.[7-9] Thiazoles possess favorable physicochemical properties, high metabolic stability, and the capacity to engage in diverse molecular interactions with biological targets owing to their aromatic heteroaromatic core and versatile substitution patterns.[10-12] The broad applicability of thiazole motifs is underscored by several clinically approved drugs and advanced drug candidates that incorporate this scaffold, highlighting its potential as a lead structure for the development of next-generation anti-inflammatory agents.[13-15]

The electronic structure of the thiazole ring supports multiple binding modalities, including π–π stacking, hydrogen bonding, and metal coordination, which are crucial for interaction with enzymes and receptors implicated in inflammatory signaling pathways.[16] Moreover, the thiazole core can function as a bioisostere for other heterocyclic systems, enabling rational optimization of pharmacokinetic and pharmacodynamic properties.[17-18] The possibility of introducing substituents at different positions (2-, 4-, and 5-) provides significant structural flexibility, facilitating fine-tuning of biological activity and drug-likeness.[19-22]

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doi: 10.5267/j.ccl.2026.3.006

Despite these promising features, the exploration of thiazole derivatives as anti-inflammatory agents is still evolving, with many structural classes and mechanisms of action yet to be fully elucidated. Therefore, a comprehensive review that integrates structural classification, structure–activity relationships (SAR), mechanistic insights, and translational potential is timely and necessary. In this review, we systematically examine the current landscape of thiazole-based anti-inflammatory compounds, emphasizing key SAR trends, biological evaluation strategies, and future directions that may accelerate the discovery of safer and more effective anti-inflammatory therapeutics.

2. Classification of thiazole-based anti-inflammatory agents

Thiazole-based anti-inflammatory agents can be broadly classified into several structural classes, each contributing distinct pharmacological properties. Simple thiazoles and thiazol-2-ones represent fundamental scaffolds, while thiazolidines introduce greater structural flexibility and diverse substitution patterns (Fig. 1). Condensed thiazole systems, including fused heterocycles, often enhance biological activity through increased rigidity and extended π-conjugation. Hybrid thiazole-containing molecules further expand therapeutic potential by combining multiple pharmacophores, enabling multi-target anti-inflammatory effects.

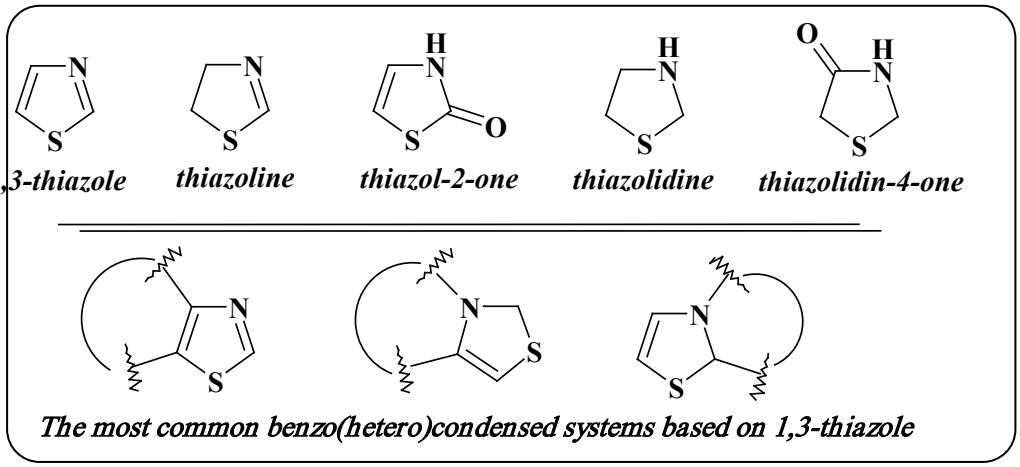


Fig. 1. Diversity of thiazole-based scaffolds as structural frames for search of potential anti-inflammatory agents.

2.1. Thiazoles, thiazolines and thiazol-2-ones

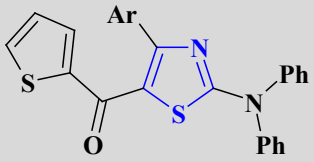
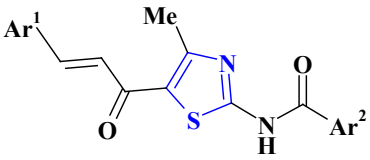
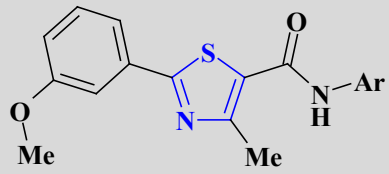
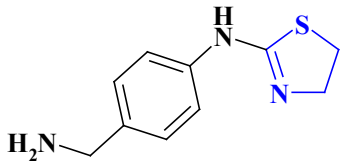
Thiazole derivatives represent one of the most prominent and widely studied scaffolds in the development of anti-inflammatory agents. Their importance stems from the unique electronic distribution of the thiazole ring and the ability to introduce diverse substituents at the 2-, 4-, and 5-positions.[23] This substitution flexibility enables systematic modulation of electronic, steric, and lipophilic properties, thereby allowing medicinal chemists to tailor binding interactions with a wide range of inflammation-related targets.[24] As a result, thiazole derivatives have been explored extensively in both preclinical and clinical contexts, demonstrating broad potential for therapeutic application.

Thiazol-2-ones, which incorporate a carbonyl functionality at the 2-position, form a particularly significant subclass of thiazole-based compounds. The presence of the carbonyl group substantially enhances the scaffold's ability to engage in hydrogen bonding and dipolar interactions with protein targets.[25] Consequently, thiazol-2-ones often exhibit improved target affinity and more robust inhibitory profiles compared to unsubstituted thiazoles. This feature makes them highly relevant for enzyme inhibition and receptor modulation, particularly in pathways associated with inflammatory responses. Moreover, the carbonyl group can act as a hydrogen bond acceptor, facilitating specific interactions within the active site of enzymes such as cyclooxygenases and lipoxygenases.[26]

In many cases, thiazole derivatives have shown promising inhibitory activity against cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, or other key mediators of inflammation (Table 1).[27,28] Notably, thiazol-2-carboxamide derivatives display improved selectivity profiles, which is a critical consideration in anti-inflammatory drug development due to the need to minimize gastrointestinal and cardiovascular adverse effects commonly associated with nonselective COX inhibition.[29] The ability of thiazoles and thiazol-2-ones to selectively target specific isoforms of COX or LOX may provide a therapeutic advantage by reducing off-target interactions and improving the overall safety margin.

Beyond COX/LOX inhibition, thiazole scaffolds have been investigated as inhibitors of inducible nitric oxide synthase (iNOS), an enzyme that plays a central role in the pathogenesis of inflammatory diseases. Thus, a group of *N*-benzyl- and *N*-phenyl-2-amino-4,5-dihydrothiazoles were investigated as potential human inducible NOS inhibitors (Table 1).[30] Conversely, the introduction of hydrophilic substituents, such as hydroxyl or aminomethylyne groups, can improve aqueous solubility and reduce cytotoxicity, thereby enhancing the drug-like properties of these molecules.

Table 1. Thiazole and thiazoline derivatives as porential anti-inflammatory agents.

Structure	Mechanism of action	Anti-inflammatory activity	Reference
 **Ar** = 4-Me-C_6H_4	Dual COX-2/5-LOX inhibition	Compound showed the most efective COX-2 and 5-LOX dual inhibitin activity with IC_{50} values of 0.09 μM and 0.38 μM, respectively. Also, it made significant decrease (60.82%) in the carrageenan-induced edema in male Wistar rats.	Jacob and Manju, 2020[27]
 **Ar¹** = C_6H_5, **Ar²** = 3,4,5-MeO-C_6H_2 **Ar¹** = 4-MeO-C_6H_4, **Ar²** = 4-Me-C_6H_4	5-LOX inhibition	The most active compounds with IC_{50} values of 0.07 ± 0.02 μM and 0.08 ± 0.05 μM were better 5-LOX inhibitors than the positive control, Zileuton (IC_{50} = 1.05 ± 0.03 μM). SAR analysis revealed that the presence of methoxy/methyl groups causes to the synergistic inhibitory effect.	Sinha *et al.*, 2019[28]
 **Ar** = 4-*t*-But-C_6H_4	COX-1/COX-2 inhibition	The most efective compound showed potent activity against the COX-1 and COX-2 enzymes with an IC_{50} of 0.239 μM and 0.191 μM, respectively, with a selectivity ratio of 1.25. IC_{50} values against normal cell lines LX-2 and Hek293t were 203.71 ± 1.89 and 116.96 ± 2.05 μM, respectively.	Hawash *et al.*, 2023[29]
	iNOS inhibition	Among series of 2-aminophenylthiazoles, an aminomethyl derivative showed the modest inhibitory activity against NOS isoforms with IC_{50} = 19 μM in human HT1080 cell line.	Minhas *et al.*, 2019[30]

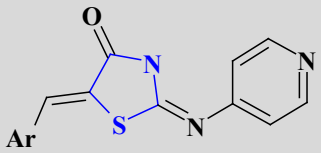
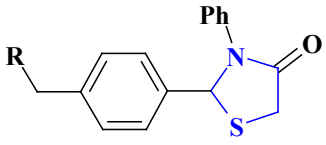
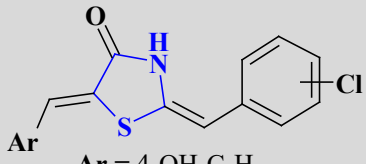
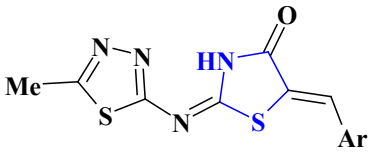
In summary, thiazoles, thiazoles and thiazol-2-ones provide a versatile and highly tunable scaffold for the design of anti-inflammatory agents. The structural diversity achievable through substitution at multiple positions enables precise optimization of potency, selectivity, and pharmacokinetic behavior. Thiazol-2-ones, in particular, offer enhanced hydrogen bonding and improved target affinity, which translate into promising inhibitory profiles against COX, LOX, and iNOS. Consequently, they remain a key focus in the ongoing development of safer and more effective anti-inflammatory therapeutics.

2.2 Thiazolidines and related structures

Thiazolidine derivatives, including thiazolidinones, represent an important and structurally distinct class of anti-inflammatory agents. Unlike aromatic thiazoles, thiazolidines contain a saturated five-membered ring, which introduces a different conformational landscape and enhances the flexibility of the scaffold. This structural difference enables thiazolidines to adopt diverse conformations and binding orientations within biological targets, which is particularly valuable when designing molecules for complex inflammatory pathways.[31,32] Consequently, thiazolidine-based compounds are frequently investigated for dual cyclooxygenase (COX) and/or lipoxygenase (LOX) inhibition, as well as for their ability to modulate broader inflammatory signaling cascades (Table 2).[33-36]

The thiazolidine scaffold offers multiple sites for functionalization, allowing medicinal chemists to systematically optimize pharmacological properties. Common structural modifications include the introduction of amide, sulfonamide, and heteroaromatic fragments, which can significantly influence potency, selectivity, and target engagement. For example, amide substitution often improves hydrogen bonding interactions with key residues in enzyme active sites, while sulfonamide groups can increase water solubility and enhance binding affinity through additional polar contacts. Heteroaromatic fragments may further strengthen π–π stacking and hydrophobic interactions, contributing to improved receptor binding. In addition to improved target interactions, thiazolidinone derivatives frequently demonstrate favorable pharmacokinetic properties. Their reduced aromaticity compared to thiazoles often leads to enhanced metabolic stability, decreased risk of oxidative metabolism, and improved overall drug-like behavior.[37,38] This profile supports their potential for oral administration and prolonged systemic exposure, which are desirable attributes for chronic inflammatory conditions.

Table 2. Thiazolidin(on)es and related structures with anti-inflammatory activity.

Structure	Mechanism of action	Anti-inflammatory activity	Reference
 **Ar** = 3-NO_2-C_6H_4	COX-2 inhibition	Compound emerged as most potent inhibitor against COX-2 with IC_{50} of 17.32±1.06 µM. In RAW 264.7 cells, it demonstrated dose-dependent suppression of mitochondrial superoxide generation at concentrations of 10 and 20 µM.	Singh *et al*., 2025[33]
 **R** = 4-Br-C_6H_4-$COCH_2$	COX-2 inhibition	Compounds exhibited the highest inhibitory activities against COX-2 with IC_{50} value of 0.06 µM. The results of the docking study into the active site of COX-2 revealed good fitting and correlation with the results of the in vitro COX-2 inhibition assay.	Mekhlef *et al*., 2023[34]
 **Ar** = 4-OH-C_6H_4, 2,5-di-MeO-C_6H_3	Suppression of pro-inflammatory cytokines (TNF-a, IL-6)	Compounds displayed the maximum suppression of TNF-a, IL-6 levels were observed in the group of animals. Docking study concluded that the compounds with the active sites of target COX2 (PDB ID: 3LN1) various possible interactions and orientations were investigated.	Archna *et al*., 2023[35]
 **Ar** = 4-Br-C_6H_4, C_6F_5	Dual COX-2 and 15-LOX inhibition	Compounds capable of inhibiting 15-LOX at 10.21 and 13.11 µM, respectively, and COX-2 at 0.1 µM. Also, compounds showed comparable *in vivo* anti-inlammatory activity to the reference drug (celecoxib) at carrageenan-induced paw edema in rats.	Omar *et al*., 2020[36]

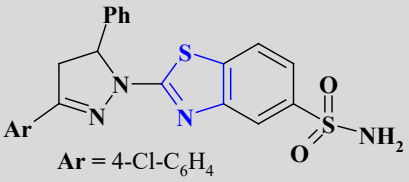
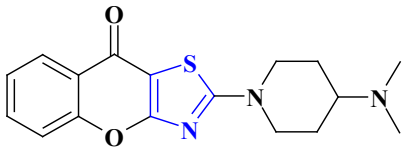
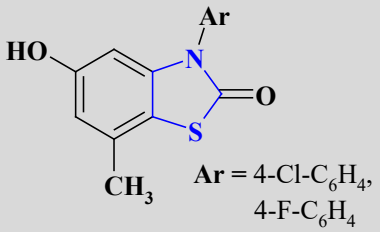
A key advantage of thiazolidinones is their conformational flexibility, which enables the scaffold to adapt to diverse enzyme pockets. This property is particularly advantageous for the design of multi-target inhibitors, as it allows the compound to engage multiple binding sites with high affinity. Furthermore, thiazolidinones often contain carbonyl and thioether functionalities, which can participate in coordination with metal ions in metalloproteins. This interaction broadens their therapeutic potential beyond classical COX/LOX targets and may provide opportunities for targeting metalloproteinases and other metal-dependent inflammatory enzymes. Such versatility underscores the importance of thiazolidinone scaffolds in contemporary anti-inflammatory drug discovery.

2.3 Condensed thiazole systems

Condensed thiazole systems, including fused bicyclic and polycyclic architectures, represent a structurally advanced class of thiazole-based biologically active agents.[39-41] By integrating the thiazole ring into an extended fused aromatic framework, these systems exhibit increased molecular rigidity and a larger delocalized π-electron surface, which are key determinants of molecular recognition and binding specificity.[42] Such architectural features are particularly advantageous for achieving high target selectivity, as they allow precise complementarity with well-defined enzymatic cavities involved in inflammatory processes. As a consequence of their expanded aromatic character, condensed thiazole derivatives frequently display enhanced binding affinity driven by strengthened π–π stacking, hydrophobic interactions, and van der Waals forces within enzyme active sites. These interactions are especially relevant for enzymes with hydrophobic channels, such as cyclooxygenases and lipoxygenases, where aromatic surface matching plays a decisive role in ligand stabilization.

Numerous fused thiazole derivatives have demonstrated significant anti-inflammatory and antioxidant activities, particularly in experimental models of chronic inflammation and oxidative stress–associated pathologies (Table 3).[43-46] In addition, fused thiazole frameworks can more effectively mimic the three-dimensional arrangement of natural ligands of enzymes such as cyclooxygenase-2 (COX-2) and lipoxygenase (LOX). Such structural mimicry has been associated with enhanced isoform selectivity, particularly toward COX-2, while simultaneously reducing interactions with off-target proteins.[47] Improved selectivity is a crucial consideration in anti-inflammatory drug development, as it directly correlates with a lower incidence of adverse effects.

Table 3. Condensed heterosystems based on thiazole that possessed anti-inflammatory action.

Structure	Mechanism of action	Anti-inflammatory activity	Reference
 Ar = 4-Cl-C_6H_4	COX-2 inhibition	Compound inhibited carrageenan-induced edema by 49.1% (celecoxib: 50.2%) at 20 mg/kg. It suppressed COX-2 activity (IC_{50}= 0.28 μM) and TNF-α production (78.4%) without ulcerogenicity (ulcer index < 2).	Mishra *et al.*, 2025[43]
	Suppression of pro-inflammatory cytokines (TNF-a, IL-6)	Compounds exhibites potent suppression on the production of IL-6 (IC_{50} =. 12.62 μM) but weaker inhibition on TNF-a (IC_{50} = 38.62 μM).	Tan *et al.*, 2024[44]
 Ar = 4-Cl-C_6H_4, 4-F-C_6H_4	Not studied	The results of anti-inflammatory activity screening on carrageenan-induced rat paw edema method allow to identify compounds with the persentage of inhibition 48.3-51.8% that exceed the compared drug Ibuprofen (40.2%)	Chaban *et al.*, 2020[46]

From a pharmacokinetic standpoint, condensed thiazole systems often exhibit superior metabolic stability compared to monocyclic thiazole derivatives.[48] Their rigid and compact structures are generally less susceptible to oxidative metabolism mediated by cytochrome P450 enzymes, resulting in slower metabolic clearance and prolonged biological half-life. Taken together, the combination of high potency, enhanced selectivity, antioxidant capacity, and improved metabolic stability highlights condensed thiazole systems as promising scaffolds for the development of next-generation anti-inflammatory agents.

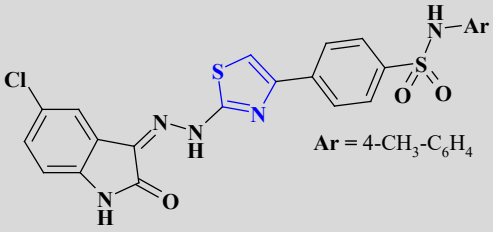
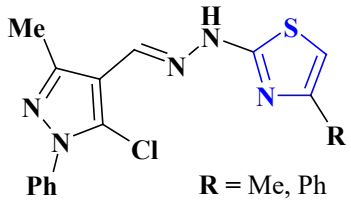
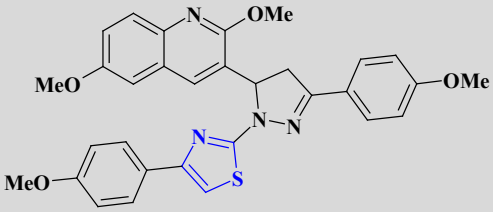
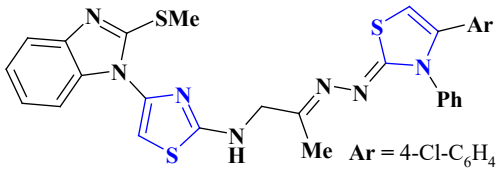
2.4 Hybrid thiazole-containing molecules

Hybrid molecules that integrate thiazole cores with additional pharmacophoric fragments represent a powerful and rational strategy for achieving multi-target activity in the treatment of inflammatory disorders. This design concept relies on combining complementary bioactive motifs within a single molecular entity, enabling the simultaneous modulation of multiple pathogenic pathways involved in inflammation. Such an approach has gained increasing attention as a means to overcome the limitations of single-target anti-inflammatory agents. Thiazole-based hybrid molecules frequently incorporate fragments with well-established anti-inflammatory and/or antioxidant or neuroprotective properties, including indole, pyrazole, coumarin, and phenolic moieties.[49-52] These pharmacophores contribute distinct biological functions and can synergistically enhance the overall therapeutic efficacy of the hybrid compounds.

The strategic selection of partner fragments is therefore critical for achieving balanced and multifunctional activity. The incorporation of multiple pharmacophoric units allows hybrid thiazole derivatives to interact concurrently with diverse molecular targets implicated in inflammatory processes. In particular, many hybrids have demonstrated the ability to modulate cyclooxygenase (COX) and lipoxygenase (LOX) enzymes (Table 4),[53,54] while simultaneously influencing transcription factors such as nuclear factor kappa B (NF-κB) and attenuating oxidative stress through radical-scavenging mechanisms. This multi-pathway modulation is especially beneficial in chronic inflammatory conditions characterized by complex and interconnected signaling networks.

In addition to enhanced pharmacodynamic profiles, hybridization strategies can significantly improve the pharmacokinetic and drug-like properties of thiazole-based compounds. By combining fragments with complementary physicochemical characteristics, medicinal chemists can optimize solubility, membrane permeability, and metabolic stability. For example, the attachment of hydrophilic moieties may improve aqueous solubility and bioavailability, whereas rigid aromatic or heteroaromatic fragments can enhance membrane penetration and reduce metabolic clearance.[55] Furthermore, molecular hybridization may reduce the likelihood of off-target toxicity and drug resistance by distributing biological activity across multiple targets rather than relying on high-affinity inhibition of a single enzyme. This balanced mode of action often translates into improved safety profiles and broader therapeutic windows.

Table 4. Thiazole-containing hybrid compounds with promising anti-inflammatory activity.

Structure	Mechanism of action	Anti-inflammatory activity	Reference
	COX-2 inhibition	Compound was the most active anti-inflammatory candidate and exhibited higher edema inhibition (EI = 38.50 %) than that recorded by celecoxib (EI = 34.58%). Molecular docking study showed good fitting into COX-2 enzyme binding site with docking energy scores -11.45 kcal/mol.	Alkorbi *et al*., 2025[49]
	COX-1/2 inhibition	Compounds exhibited significant inhibition rates in a carrageenan-induced paw edema model of 66.67% and 73.08%, respectively. Molecular docking studies revealed strong and favorable binding interactions with the active sites of COX-1 and COX-2 enzymes.	Abdul-Malik *et al*., 2026[50]
	Dual COX-2/15-LOX inhibition	Quinoline/pyrazoline/thiazole hybrid disclosed marked inhibitory activity against 15-LOX and strong inhibitory to COX-2 (IC_{50}= 0.201 µM, SI = 14.42) that revealed more potency and selectivity outperforming celecoxib (IC_{50} = 0.512 µM, SI = 4.28).	Hegazy *et al*., 2024[53]
	Dual COX-2/15-LOX inhibition	Benzimidazole-thiazole hybrid was the most potent dual COX-2 (IC_{50} = 0.045 µM, SI = 294) inhibitor compared to celecoxib (COX-2; IC50 = 0.045 µM, SI = 327), with double inhibitory activity versus 15-LOX enzyme (IC_{50} = 1.67 µM) relative to quercetin (IC_{50} = 3.34 µM).	Maghraby *et al*., 2020[54]

3. Mechanisms of anti-inflammatory action

Thiazole derivatives exhibit anti-inflammatory activity through multiple complementary mechanisms, reflecting their versatile interaction with key biological targets (**Fig. 2**). They can suppress the production of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6) and inhibit critical signaling pathways such as NF-κB, thereby reducing the expression of inflammatory genes. In addition, these compounds may inhibit enzymes like COX-2 and iNOS, leading to decreased levels of prostaglandins and nitric oxide. Their antioxidant properties and ability to modulate immune cell activation further contribute to the overall attenuation of the inflammatory response.

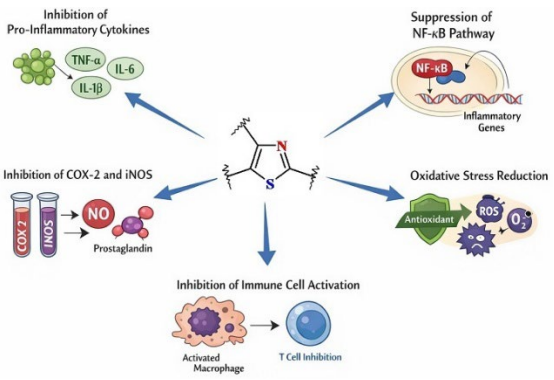
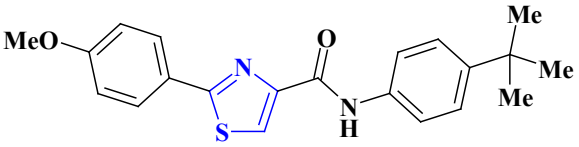


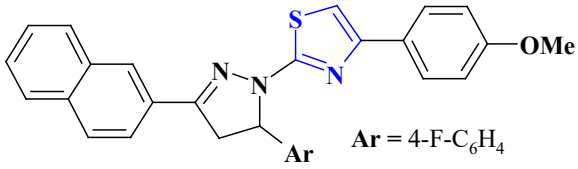
Fig. 2. Possible anti-inflammatory mechanisms of thiazole derivatives.

3.1 COX/LOX inhibition

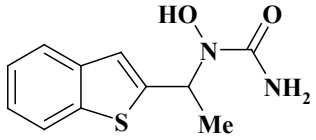
The cyclooxygenase (COX) and lipoxygenase (LOX) pathways are central to the biosynthesis of key pro-inflammatory mediators, including prostaglandins, thromboxanes, and leukotrienes, which play a pivotal role in the initiation and progression of inflammatory responses.[56] Dysregulation of these enzymatic cascades has been implicated in a wide range of acute and chronic inflammatory disorders. Consequently, pharmacological modulation of COX and LOX enzymes remains a major therapeutic strategy in anti-inflammatory drug development. Numerous thiazole derivatives have been reported to inhibit COX-1, COX-2 or 5-lipoxygenase (5-LOX), leading to a marked reduction in the production of pro-inflammatory eicosanoids (Fig. 3).[57-59] This inhibition results in the attenuation of inflammatory signaling and a decrease in tissue damage associated with excessive mediator release. Both monocyclic and fused thiazole scaffolds have demonstrated activity across these targets, highlighting their structural adaptability.



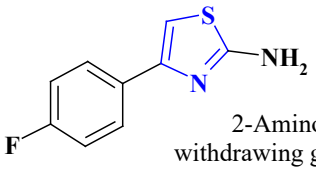
The most potent, with an inhibitory activity percentage at 5 μM concentration of 81.5 and 58.2% against COX-2 and COX-1, respectively (Hawash *et al*., 2024) [57]



The most active candidate showed nearly equpotent COX-1 inhibition (IC_{50} = 38.76nM) compared to the non-selective reference drug Indometacin (IC_{50} = 35.72nM) (Mohammed *et a*l., 2024) [58]



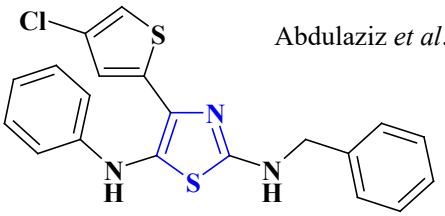
Zileuton
(the only drug currently marketed that targets 5-LOX enzyme, IC_{50} = 1μM)



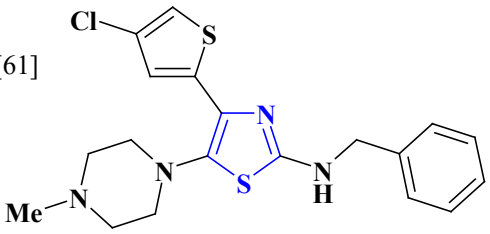
2-Amino-4-aryl thiazole derivatives with an electron withdrawing group (fluoro substitution) at the *p*-position adjacent to the benzene ring is the most active 5-LOX inhibitor with an IC_{50} of 10 μM (Sinha *et al*., 2016) [59]

Fig. 3. Substituted 1,3-thiazoles as potent COX-1, COX-2 or 5-LOX inhibitors.

In recent years, increasing attention has been directed toward the development of dual COX/LOX inhibitors, which are designed to simultaneously suppress both enzymatic pathways. This approach is particularly attractive because selective inhibition of COX enzymes alone can lead to metabolic shunting of arachidonic acid toward leukotriene biosynthesis, thereby sustaining inflammation. Dual inhibition can mitigate this effect and provide more comprehensive anti-inflammatory efficacy.[60] Importantly, dual COX/LOX inhibitors have been associated with a reduced incidence of gastrointestinal adverse effects compared to selective COX-2 inhibitors. By maintaining a balanced modulation of eicosanoid pathways, these compounds may offer improved safety profiles, especially during long-term treatment of chronic inflammatory conditions. As a result, thiazole-based dual inhibitors are considered promising alternatives to conventional nonsteroidal anti-inflammatory drugs (Fig. 4).[53,61]



Abdulaziz *et al*., **2024** [61]



IC_{50} (COX-2) = 0.76μM,
IC_{50} (COX-1) = 94.33μM, SI = 124,
IC_{50} (5-LOX) = 38.45μM

IC_{50} (COX-2) = 0.83μM,
IC_{50} (COX-1) = 93.41μM, SI = 112,
IC_{50} (5-LOX) = 23.08μM

Fig. 4. An effective dual COX-2/5-LOX inhibitors based on 1,3-thiazole core.

Overall, the capacity of thiazole-based compounds to modulate both COX and LOX pathways underscores their versatility and therapeutic potential. Their structural flexibility allows the design of selective or dual inhibitors with optimized efficacy and safety profiles. These features position thiazole derivatives as valuable scaffolds for the development of next-generation anti-inflammatory agents targeting eicosanoid-mediated inflammation.

3.2 Modulation of NF-κB, MAPK, and JAK/STAT pathways

Thiazole-based compounds have been shown to effectively modulate key intracellular signaling cascades involved in the regulation of inflammatory gene expression. Among these, inhibition of nuclear factor kappa B (NF-κB) activation represents one of the most extensively studied mechanisms. Suppression of NF-κB signaling prevents the transcription of a broad range of pro-inflammatory mediators, including cytokines, chemokines, adhesion molecules, and inducible enzymes such as inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) (Fig. 5).[62,63] As a consequence, thiazole derivatives can significantly reduce both the initiation and propagation of inflammatory responses.

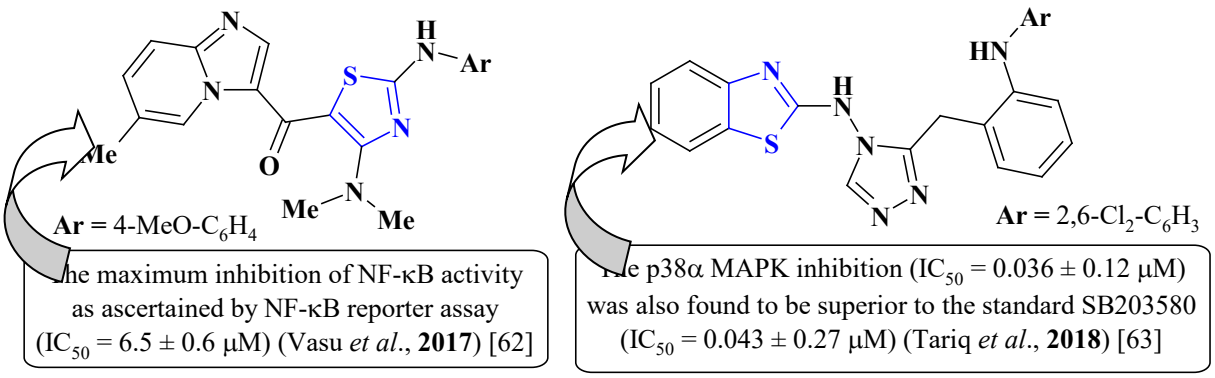


Fig. 5. Impact of thiazoles on NF-κB and MAPK signaling pathways.

In addition to NF-κB, thiazole-based compounds have been reported to influence other critical signaling pathways, notably the mitogen-activated protein kinase (MAPK) and Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathways (**Fig. 6**).[64,65] Modulation of MAPK signaling, including the ERK, JNK, and p38 branches, can attenuate cytokine-induced cellular activation and downstream inflammatory gene expression. Similarly, interference with JAK/STAT signaling reduces cytokine-mediated signal amplification, thereby limiting the sustained inflammatory response. These combined effects contribute to the broad anti-inflammatory potential of thiazole derivatives.

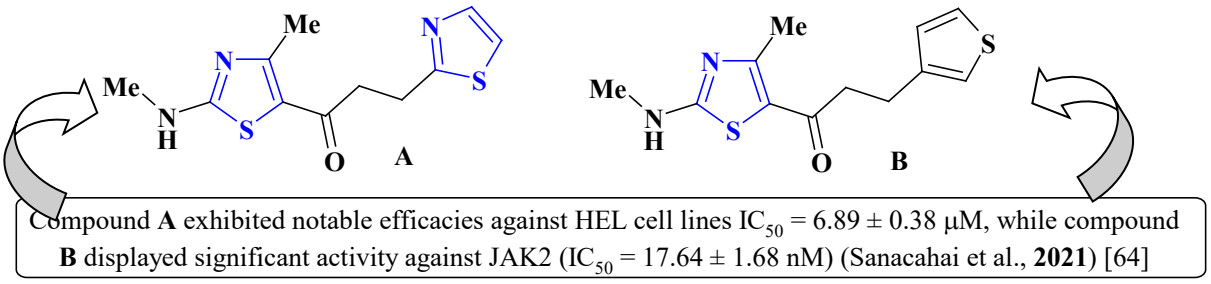


Fig. 6. Impact of thiazoles on JAK/STAT signaling pathways.

Importantly, the structural versatility of the thiazole scaffold enables rational optimization for multi-target activity. Substituent variation and hybridization strategies allow thiazole-based molecules to interact with diverse protein targets involved in signal transduction, transcriptional regulation, and enzyme activity. This adaptability not only enhances pharmacodynamic efficacy but also supports the development of compounds with balanced activity profiles and reduced likelihood of resistance or compensatory pathway activation. Collectively, these features highlight thiazole scaffolds as highly suitable candidates for network-oriented anti-inflammatory drug discovery.

3.3 Suppression of pro-inflammatory cytokines

Thiazole derivatives consistently demonstrate the capacity to attenuate pro-inflammatory cytokine production, with numerous studies reporting significant reductions in TNF-α, IL-1β, and IL-6 levels across both cellular and animal models of inflammation (Fig. 7).[66,67] This cytokine-lowering effect is frequently accompanied by suppression of key upstream signaling cascades, particularly NF-κB and MAPK pathways, thereby supporting a mechanistic link between pathway modulation and downstream cytokine inhibition.[68] Collectively, these findings highlight the therapeutic potential of thiazole-based scaffolds for cytokine-driven inflammatory disorders, including rheumatoid arthritis, inflammatory bowel disease, and neuroinflammatory conditions, where dysregulated cytokine signaling is a central pathogenic feature.

In addition to their inhibitory effects on pro-inflammatory mediators, certain thiazole derivatives have been shown to enhance anti-inflammatory cytokine responses, notably by upregulating IL-10 production (Fig. 7).[69] Such immunomodulatory activity suggests that these compounds may not only suppress inflammation, but also actively promote

resolution and restoration of immune homeostasis. This dual modulatory profile is particularly relevant in chronic inflammatory states, where a shift toward a pro-resolving cytokine milieu is crucial for long-term therapeutic efficacy.

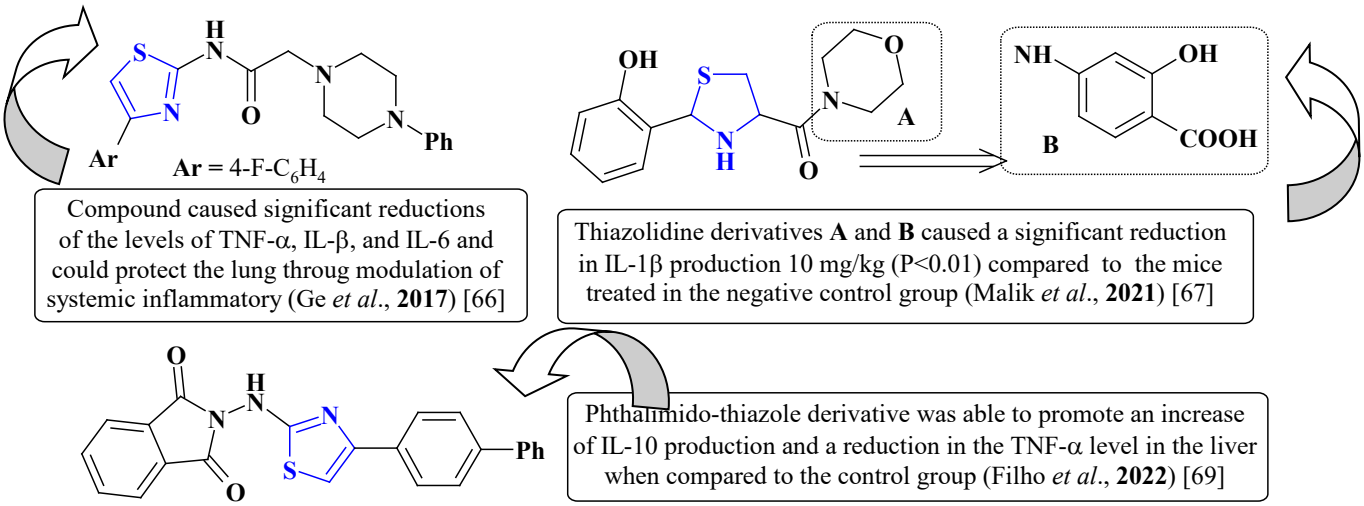


Fig. 7. Thiazole and thiazolidine derivatives as suppressors of pro-inflammatory cytokines.

Moreover, emerging evidence indicates that thiazole scaffolds may influence additional immunoregulatory pathways, including the balance of M1/M2 macrophage polarization and the regulation of T-cell differentiation, further expanding their potential beyond mere cytokine suppression.[70] These pleiotropic effects underscore the value of thiazole-based compounds as multifunctional anti-inflammatory agents, capable of targeting both innate and adaptive immune responses.

3.4 Antioxidant contribution to anti-inflammatory activity

Oxidative stress is closely intertwined with inflammation, forming a self-amplifying loop that exacerbates cellular and tissue damage in chronic disease settings.[71] Many thiazole compounds have demonstrated notable antioxidant properties, including direct radical scavenging, inhibition of lipid peroxidation, and modulation of endogenous antioxidant defenses such as superoxide dismutase (SOD), catalase (CAT), and glutathione-related system.[72-74] This dual anti-inflammatory and antioxidant activity may provide additive protection in chronic inflammatory states, where oxidative stress is not only a consequence but also a driver of pathology.

Antioxidant activity can also indirectly attenuate inflammatory signaling by decreasing reactive oxygen species (ROS)-mediated activation of NF-κB and MAPK pathways, thereby reducing the expression of pro-inflammatory genes.[75] In this context, thiazole derivatives that combine radical scavenging with pathway inhibition may more effectively disrupt the oxidative stress–inflammation cycle than agents acting on a single target. Consequently, compounds that combine both anti-inflammatory and antioxidant effects may offer superior therapeutic outcomes compared with agents targeting only one pathway, particularly in diseases characterized by persistent oxidative and inflammatory insults, such as neurodegenerative disorders, cardiovascular diseases, and chronic autoimmune conditions.[76,77] The synergistic modulation of oxidative and inflammatory networks by thiazole scaffolds highlights their promise as multifunctional drug candidates and supports further optimization through structure–activity relationship studies.

4. *In vitro* assessment of anti-inflammatory activity in thiazole scaffolds

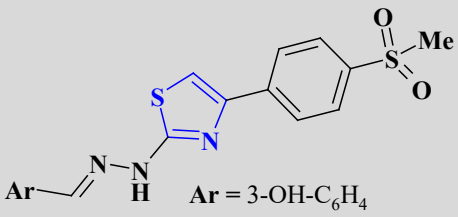
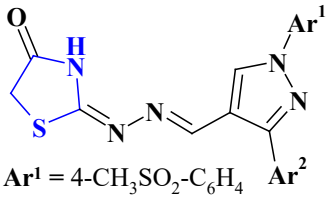
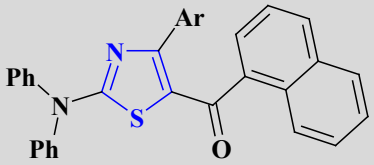
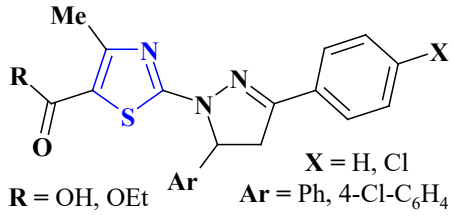
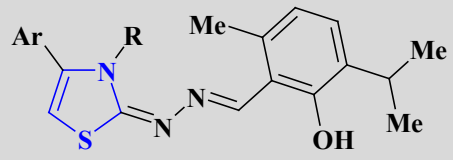
In vitro assessment of anti-inflammatory activity in thiazole scaffolds encompasses several complementary experimental strategies to provide a comprehensive evaluation of their pharmacological potential. Enzymatic inhibition assays, including COX, LOX, and iNOS, allow direct measurement of the compounds' effects on key inflammatory mediators. Cellular models facilitate quantification of cytokine production, revealing the influence of thiazole derivatives on immune signaling pathways. Antioxidant assays, such as DPPH, ABTS, and FRAP, are employed as complementary tools to assess radical scavenging and reducing capacity, highlighting potential dual therapeutic benefits. Careful methodological considerations, including appropriate controls, biological replicates, and standardized protocols, are crucial for ensuring reproducibility and reliability of results. Overall, these combined approaches provide a detailed understanding of the mechanisms by which thiazole-based compounds exert anti-inflammatory and cytoprotective effects.

4.1 Enzymatic inhibition (COX/LOX, iNOS)

Enzymatic assays remain a primary tool for assessing the anti-inflammatory potential of thiazole derivatives, as they provide direct evidence of target engagement and inhibitory efficacy. Inhibition of COX-1/2 and 5-LOX is particularly informative, because these enzymes are central to eicosanoid biosynthesis and represent validated targets for anti-inflammatory therapy. By suppressing prostaglandin and leukotriene production, thiazole-based inhibitors can reduce key mediators of inflammation, pain, and vascular responses. Studies show that thiazole and thiazol-2-one derivatives are able

to effectively inhibit COX-2 activity while maintaining relative selectivity for COX-1, which is important for reducing the risk of gastrointestinal side effects (Table 5).[78-80] Particular attention is also paid to the inhibition of lipoxygenases, in particular 5-LOX, since leukotrienes formed from arachidonic acid by the action of 5-lipoxygenase play a key role in the development of chronic inflammation and allergic reactions. It has been shown that some functionalized thiazole systems can simultaneously affect the COX and LOX pathways, which enhances their anti-inflammatory potential (Table 5).[81-83]

Table 5. Thiazole and thiazolidine derivatives that have an inhibitory effect on COX-1/2 and 5-LOX enzymes.

Structure	Mechanism of action	Anti-inflammatory activity	Reference
 **Ar** = 3-OH-C_6H_4	Selective COX-2 inhibition	Compound was found to be the most effective derivative COX-2 inhibitor with an IC_{50} value of 0.140 ± 0.006 μM. Moreover, it was seen a more potent inhibition profile at least 12-fold than nimesulide (IC_{50} = 1.684 ± 0.079 μM).	Sağlık *et al*., 2021[78]
 **Ar¹** = 4-CH_3SO_2-C_6H_4 **Ar²** = 4-CH_3-C_6H_4	Selective COX-2 inhibition	Compound inhibit COX-2 (IC_{50} = 0.349 ± 0.01 μM) and COX-1 (IC_{50} = 46.98 ± 2.01 μM) compared to reference durg celecoxib (IC_{50} COX-2 = 0.685 ± 0.03 μM; IC_{50} COX-1 = 16.5 ± 0.71 μM;). The selectivity index of thiazole derivative was SI = 134.6 in comparison with celecoxib (SI = 24.09)	Fadaly *et al*., 2023[79]
 **Ar** = 4-NO_2-C_6H_4	Dual COX-2 and 5-LOX inhibition	Compound showed equivalent COX-2 (IC_{50} = 0.07 ± 0.02 μM) inhibitory potency as that of positive control etoricoxib (IC_{50} = 0.07 ± 0.01 μM) and an enhanced selectivity index of 115.14. Also, it exhibited 5-LOX IC_{50} of 0.29 ± 0.09 μM.	Jaismy and Manju, 2021[81]
 **R** = OH, OEt **X** = H, Cl **Ar** = Ph, 4-Cl-C_6H_4	Dual COX-2 and 5-LOX inhibition	Compounds were the most potent and COX-2 selective inhibitors (IC_{50} = 0.03–0.06 μM, SI = 282.7–472.9) with high activity against 5-LOX (IC_{50} = 4.36–4.86 μM) compared to reference celecoxib (IC_{50} COX-2; 0.04 ± 0.003 μM) and quercetin (IC_{50} 5-LOX; 3.81 ± 0.26 μM).	Elgohary *et al*., 2023[82]
	Dual COX-2 and 5-LOX inhibition	Compounds displayed a group *in vitro* inhibitory activity against COX-2 (IC_{50} = 0.037-0.046 μM) nearly equal to celecoxib (IC_{50} = 0.045 μM) and selective index SI at the range of 341-379 higher than that of celecoxib (327).	El-Miligy *et al*., 2024[83]

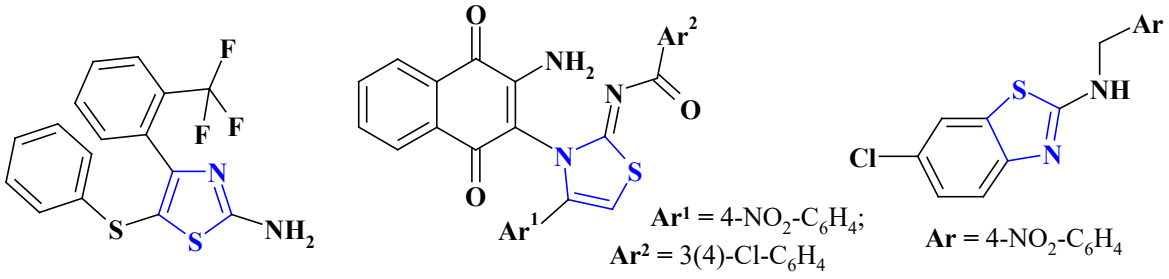
Inhibition of inducible NO synthase (iNOS) is another important aspect of *in vitro* studies. Excessive production of nitric oxide contributes to the maintenance of inflammation and tissue damage, so reducing iNOS activity is considered a promising therapeutic approach. Additional evaluation of iNOS inhibition is also relevant, since nitric oxide is a major inflammatory mediator that contributes to vasodilation, oxidative stress, and tissue damage in chronic inflammatory states.[84] Thiazole derivatives, which are able to reduce NO levels in stimulated macrophages, demonstrate pronounced anti-inflammatory efficacy.[85,86]

In general, enzymatic assays allow kinetic characterization, including determination of IC_{50} and K_i values, which are crucial for SAR analysis and for comparing the intrinsic potency of thiazole scaffolds across the different target classes. Comparative evaluation against reference drugs (e.g., diclofenac, indomethacin, celecoxib) provides important context for

potency and selectivity, and helps to identify whether thiazole derivatives offer advantages in terms of efficacy or reduced off-target effects. Moreover, kinetic parameters can reveal the mode of inhibition (competitive, non-competitive, or irreversible), which is essential for rational optimization of thiazole compounds toward improved therapeutic profiles.

4.2 Cytokine production in cellular models

Cell-based assays using macrophages, monocytes, or epithelial cells allow measurement of cytokine release (TNF-α, IL-1β, IL-6) following inflammatory stimulation, providing a functional readout of thiazole derivatives' anti-inflammatory potential.[87] These models also enable mechanistic insights into the modulation of key signaling pathways, such as NF-κB and MAPK, by assessing changes in phosphorylation status, nuclear translocation, and downstream gene expression. The cellular assays capture the integrated response of multiple pathways and cellular processes, including oxidative stress, apoptosis, and autophagy, which cannot be assessed using enzymatic assays alone. Numerous studies have shown that thiazole derivatives are able to significantly reduce the secretion of TNF-α, IL-1β, and IL-6, which play a central role in the pathogenesis of acute and chronic inflammation (Fig. 8).[88,89] Importantly, some thiazole derivatives exhibit differential effects on individual components of cytokine profiles, which opens up opportunities for more targeted immunopharmacological correction.[90] Thus, the combination of enzymatic and cellular assays is therefore essential for a comprehensive evaluation of anti-inflammatory activity and for validating the biological relevance of thiazole scaffolds identified through target-based screening.



Ganie *et al*., **2024** [88] Efeoglu *et al*., **2023** [89] Xu *et al*., **2024** [88]

Fig. 8. Structures of 1,3-thiazole derivatives that could suppress suppress the production of pro-inflammatory cytokines.

Advanced cellular models, including co-culture systems and 3D spheroids, provide additional insights into tissue-level responses, compound penetration, and cell–cell interactions that are critical in chronic inflammation.[91] These models better mimic the physiological microenvironment by incorporating multiple cell types, extracellular matrix components, and gradients of oxygen and nutrients, which can influence drug distribution and efficacy. As a result, they improve translational relevance and can help bridge the gap between *in vitro* findings and *in vivo* outcomes, making them particularly valuable for evaluating thiazole derivatives intended for complex inflammatory diseases.

4.3 Antioxidant assays as complementary tools

Antioxidant assays such as DPPH, ABTS, and FRAP complement anti-inflammatory evaluation by measuring radical scavenging and reducing capacity of thiazole derivatives, thus providing an initial indication of their ability to neutralize reactive species.[92] Since oxidative stress is a key contributor to inflammation and tissue damage, these assays help identify compounds with dual therapeutic potential, combining both anti-inflammatory and antioxidant effects. It has been proven that thiazole derivatives with pronounced radical-scavenging activity demonstrate an enhanced anti-inflammatory effect in cell models, which confirms the synergy of antioxidant and anti-inflammatory mechanisms.[93,94] Integration of antioxidant data with enzymatic and cellular anti-inflammatory results enhances the predictive value of *in vitro* screening and supports selection of lead compounds for further optimization.

Additionally, evaluation of intracellular ROS levels using fluorescent probes (e.g., DCFH-DA) can reveal whether thiazole compounds reduce oxidative stress in live cells, providing more physiologically relevant evidence than cell-free assays.[95] This approach enables mechanistic insight into whether antioxidant activity is mediated by direct radical scavenging, modulation of endogenous antioxidant enzymes, or inhibition of ROS-generating pathways such as NADPH oxidase or mitochondrial dysfunction. By combining cell-free and cell-based antioxidant assessments, researchers can better understand the multifaceted redox-modulating properties of thiazole derivatives and their contribution to overall anti-inflammatory efficacy.

4.4 Methodological considerations

Advanced techniques such as ELISA, Western blotting, and qPCR (Fig. 9) are essential for mechanistic characterization of thiazole derivatives, enabling quantitative assessment of cytokines, inflammatory enzymes, and signaling proteins at both protein and transcript levels. These methods provide insight into how thiazole compounds modulate key inflammatory

pathways, including NF-κB, MAPK, and STAT signaling, by allowing measurement of phosphorylation states, nuclear translocation, and downstream gene expression. Rigorous experimental design, including appropriate positive and negative controls, biological replicates, and standardized protocols, is crucial for reproducibility and for meaningful comparison of results across different studies and laboratories.

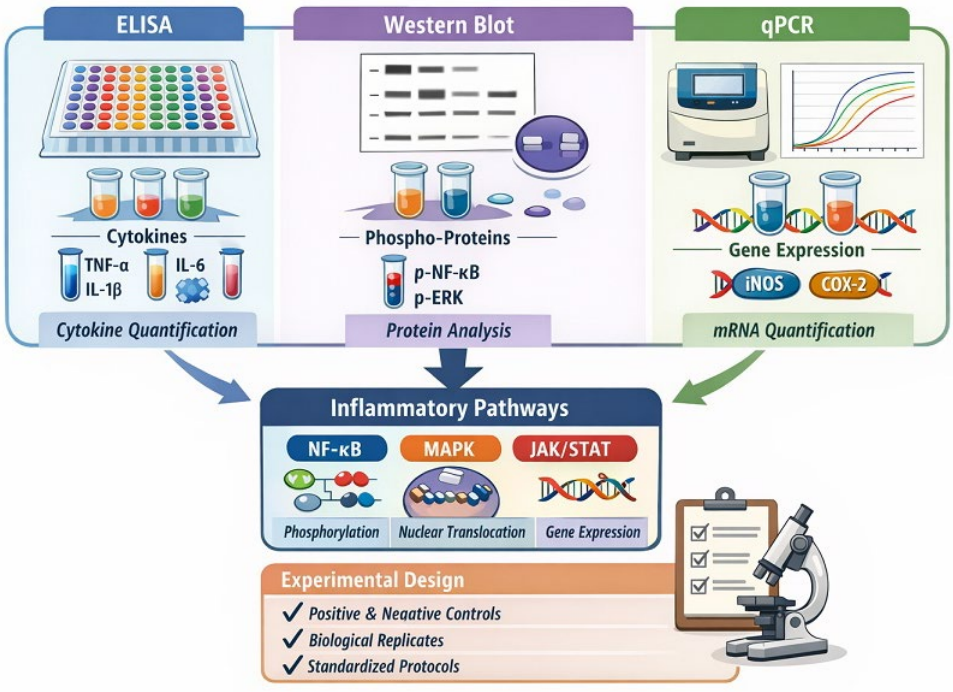


Fig. 9. Schematic representation of advanced experimental techniques used for mechanistic evaluation of thiazole derivatives.

Thus, ELISA methodology allows for accurate determination of the levels of key proinflammatory cytokines (including TNF-α, IL-1β, IL-6), prostaglandins, and other inflammatory mediators in culture media.[96] ELISA is widely used in pharmacological screening of anti-inflammatory agents, as it combines high reproducibility of results, the ability to simultaneously analyze a large number of samples, and adaptability to various cellular models of inflammation. The data obtained in this way allow not only to assess the overall anti-inflammatory potential of compounds, but also to draw conclusions about their effect on individual signaling links of the inflammatory cascade.

Western blot and real-time quantitative polymerase chain reaction (qPCR) methods provide a detailed analysis of changes in the expression of key proteins and genes involved in the development and regulation of the inflammatory process. Western blot allows for the assessment of the expression levels and degree of activation of signaling proteins, in particular COX-2, iNOS, NF-κB (p65), as well as components of MAPK cascades, including p38, ERK and JNK, which allows for the tracing of the effect of the studied compounds on the intracellular mechanisms of the inflammatory response.[97,98] At the same time, qPCR is used to quantify the mRNA levels of relevant pro-inflammatory genes, such as TNF-α, IL-1β, IL-6, COX-2 and iNOS, which allows for the establishment of the effect of compounds on the transcriptional regulation of inflammation.[99]

Proper validation of assays is also essential, including confirmation of compound stability under assay conditions and exclusion of interference with detection systems (e.g., fluorescence quenching or nonspecific binding), which is particularly relevant for heteroaromatic thiazole derivatives with potential optical or redox activity.[100] *In vitro* data should be interpreted with caution, considering limitations such as cell line specificity, concentration-dependent cytotoxicity, and differences in metabolic capacity compared with *in vivo* systems. Therefore, mechanistic findings from cellular assays should ideally be complemented by *in vivo* models and pharmacokinetic studies to confirm the translational relevance of thiazole-based anti-inflammatory candidates.

5. Perspectives for structural optimization and drug development

Current trends in the development of small molecules are focused not only on increasing biological activity, but also on creating compounds with high selectivity, optimal pharmacokinetics and a minimal side effect profile. Modern pharmacology is increasingly moving away from monotargeted approaches, preferring instead multitargeted strategies that allow for simultaneous influence on several links in pathogenesis. Such synergism provides not only a reduction in the intensity of inflammation, but also tissue protection from oxidative damage, which is key in chronic inflammatory

conditions. In this context, the thiazole core is considered as a flexible platform for constructing molecules with specified properties, allowing for the combination of different functional fragments, modification of electronic and spatial parameters, and influence on metabolic stability (Fig. 10).

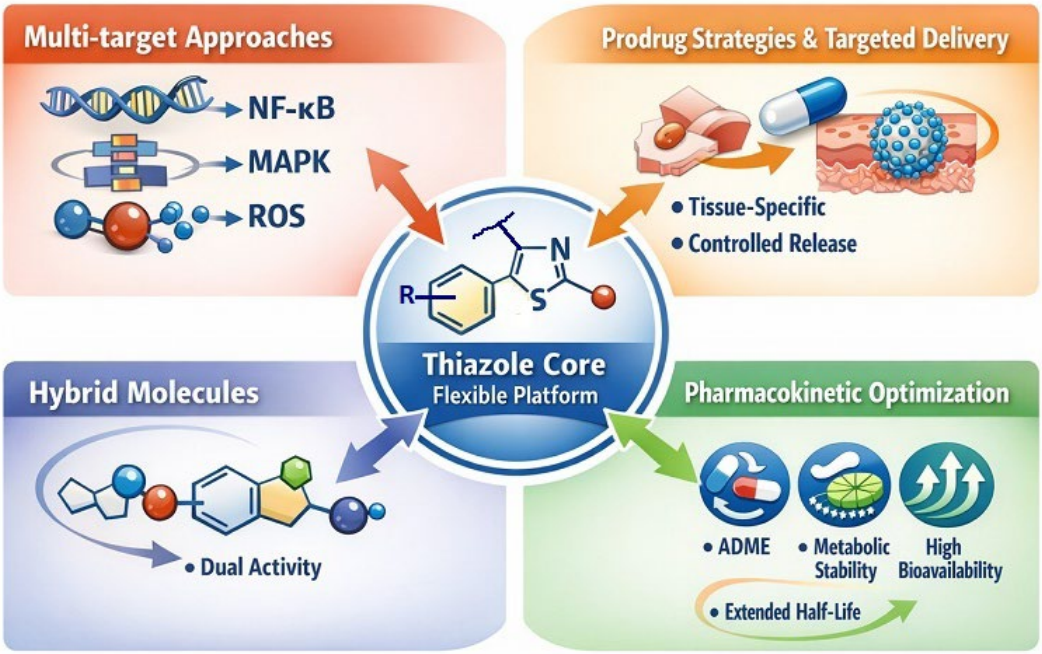


Fig. 10. Perspectives for structural optimization and drug development of thiazole derivatives as potential anti-inflammatory agents.

5.1 Multi-target approaches

Given the complexity and multifactorial nature of inflammatory diseases, multi-target compounds are increasingly recognized as promising therapeutic solutions capable of addressing interconnected pathogenic pathways. Thiazole derivatives are particularly well suited for this strategy, as their structural versatility allows rational design of molecules that can simultaneously inhibit COX/LOX enzymes, modulate NF-κB and MAPK signaling cascades, and mitigate oxidative stress through redox modulation.[65,101] This multi-target approach aligns with the polypharmacology paradigm and may reduce the risk of tolerance development and dose-limiting side effects commonly associated with single-target anti-inflammatory agents.

In addition to controlling inflammation, multi-target thiazole-based compounds can potentially address relevant comorbidities, such as oxidative stress–driven tissue damage, neurodegenerative processes, and metabolic dysregulation, which frequently coexist with chronic inflammatory disorders.[102,103] By integrating anti-inflammatory, antioxidant, and signaling-modulatory activities within a single chemical entity, this approach may improve therapeutic outcomes, enhance patient compliance, and reduce the need for combination therapies. Consequently, multi-target thiazole derivatives represent an attractive direction for the development of next-generation anti-inflammatory agents with broader and more durable clinical efficacy.

5.2 Prodrug strategies and targeted delivery

Prodrug design and advanced drug delivery systems represent effective strategies for overcoming key pharmacokinetic limitations of thiazole derivatives, such as poor aqueous solubility, limited permeability, and low oral bioavailability. Prodrug strategies allow for temporary modification of a drug-like molecule, improving its pharmacokinetic properties without losing its pharmacodynamic profile. By temporarily masking polar functional groups or introducing cleavable linkers, prodrug approaches can improve absorption and systemic exposure while enabling controlled release of the active compound at the target site.[104] In turn, esterification of carboxyl or hydroxyl groups can increase membrane permeability and provide prolonged release of the active form in tissues. In addition, ester derivatives often function as prodrugs,[105] providing controlled and prolonged release of the active form in tissues due to enzymatic hydrolysis at the site of action. This approach allows to reduce systemic side effects, maintain stable drug concentrations in the blood or tissues and increase the effectiveness of therapy, especially in the treatment of chronic diseases associated with inflammatory and oxidative processes.

In parallel, lipid-based carriers, polymeric nanoparticles, and stimuli-responsive delivery systems have emerged as powerful platforms for targeted delivery of thiazole-based compounds to inflamed tissues, thereby improving therapeutic index and reducing systemic toxicity. The use of nanotechnology (liposomes, polymer nanoparticles, solid-dispersed systems) allows to increase the local concentration of the drug in the affected tissues.[106] At the same time, targeted delivery strategies can also minimize off-target effects and increase local drug concentration at sites of inflammation, which is particularly relevant for potent multi-target thiazole derivatives.

Modern approaches also include the use of "smart" carriers that respond to pH, oxidative stress, or enzymatic markers of inflammation, ensuring selective drug release in the area of pathology. For example, pH-sensitive nanoparticles can exploit the acidic microenvironment of inflamed tissues to trigger site-specific drug release, while ligand-functionalized systems can selectively bind to inflammatory markers such as selectins, integrins, or overexpressed cell-surface receptors on activated immune cells.[107] These advanced delivery approaches not only enhance the pharmacological performance of thiazole derivatives but also expand their applicability to chronic inflammatory diseases requiring sustained and localized therapeutic intervention.

5.3 Hybrid molecules

Hybridization of thiazole cores with other pharmacophores represents a powerful strategy for achieving synergistic and complementary biological effects within a single molecular framework. This approach corresponds to the concept of "one molecule – multiple targets" and is particularly promising in the development of anti-inflammatory agents with increased efficacy and selectivity. Owing to the structural versatility of the thiazole ring, hybrid molecules can be rationally designed to integrate anti-inflammatory, antioxidant, neuroprotective, or antimicrobial functionalities, thereby broadening therapeutic utility and addressing complex disease phenotypes.[108-110] Such hybrid thiazole-based compounds are particularly attractive for chronic inflammatory conditions, where multiple pathogenic mechanisms – including oxidative stress, immune dysregulation, and tissue degeneration–operate simultaneously.

In addition to enhancing efficacy, hybrid molecules can help overcome resistance or compensatory mechanisms by targeting multiple signaling pathways at once. For example, combining COX inhibition with NF-κB modulation within a single thiazole-based hybrid can provide both rapid suppression of inflammatory mediators and longer-term control of pro-inflammatory gene expression.[63,111] Also, such molecules can inhibit the activity of COX and LOX enzymes, reducing the synthesis of pro-inflammatory prostaglandins and leukotrienes, and modulate intracellular signaling pathways, in particular MAPK (p38, ERK, JNK).[112] This dual-level intervention may reduce the likelihood of tolerance development and improve durability of therapeutic responses compared with single-target agents. Overall, pharmacophore hybridization involving thiazole scaffolds offers a promising route toward next-generation multi-functional therapeutics capable of addressing inflammation and its associated comorbidities more effectively.

5.4 Pharmacokinetic optimization

Optimizing pharmacokinetic properties remains a major challenge in the development of thiazole derivatives, particularly due to issues related to limited solubility, rapid metabolism, and suboptimal membrane permeability. Strategies such as salt formation, cocrystal engineering, and targeted molecular modifications are increasingly employed to improve aqueous solubility, metabolic stability, and overall drug-like behavior of thiazole-based compound.[113] In addition, micro- and nanodispersion technologies, including micronization, nanocrystals, solid dispersions, and nanodelivery systems, are widely used to increase the surface area of particles and accelerate the dissolution process.[114] A balanced optimization approach is essential to ensure adequate systemic exposure while minimizing toxicity and off-target accumulation, especially for multi-target thiazole scaffolds with high intrinsic potency.

The stability of molecules in biological environments depends on their metabolic vulnerability. Modification of lipophilicity, protection of metabolically labile groups, or introduction of biostable isosteres can significantly extend the half-life and reduce the formation of toxic metabolites. In particular, modification of lipophilicity is one of the key factors in optimizing the pharmacokinetic properties of drug compounds, as it significantly affects absorption, distribution, metabolism, and excretion (ADME).[115] Increasing lipophilicity usually contributes to better membrane permeability and absorption, but excessive lipophilicity can lead to reduced aqueous solubility, increased accumulation in fat depots, and enhanced metabolic biotransformation, particularly with the participation of cytochrome P450 enzymes.

Protection of metabolically labile functional groups is an important strategy for optimizing the pharmacokinetic properties of drug compounds, as it allows to reduce the rate of their enzymatic biotransformation and metabolic clearance.[116] Masking or replacing such groups that are subject to rapid oxidation or hydrolysis contributes to increased metabolic stability and prolongation of the half-life. In addition, reducing the formation of reactive or toxic metabolites has a positive effect on the safety profile of the compound. In contrast, targeted bioisosteric substitutions affect the rate of enzymatic metabolism and contribute to the formation of more metabolically stable derivatives, which reduces the risk of a toxic biotransformation profile and improves the pharmacokinetic properties of the compounds.[117] Such structural modifications contribute to the formation of more metabolically stable derivatives with a prolonged half-life and reduced

systemic clearance. An important advantage of bioisosteric substitutions is also the reduction in the likelihood of the formation of reactive or toxic metabolites, which positively affects the safety profile of the compounds.

Among the effective approaches, the use of solid-dispersed systems, where active pharmaceutical ingredients are dispersed in hydrophilic polymer matrices, lipid carriers, including solid-lipid nanoparticles and microemulsions, as well as inclusion complexes with cyclodextrins, which form constantly stable water-soluble complexes with drug molecules.[118] These technologies allow to significantly increase the solubility in the aqueous environment, reduce the variability of absorption, improve the rate of achieving therapeutic concentrations and maintain stable plasma levels of the active ingredient for a long time. In addition, the use of such systems can reduce the irritating effect on the gastrointestinal tract, protect the compound from premature metabolism and contribute to a more predictable pharmacokinetic profile. Together, these strategies highlight the importance of integrating medicinal chemistry, formulation science, and pharmacokinetic profiling to advance thiazole-based anti-inflammatory and antioxidant agents toward clinical applicability.

6. Conclusions

Thiazole-based scaffolds – including thiazoles, thiazolines, thiazol-2-ones, thiazolidines, condensed thiazole systems, and hybrid derivatives – demonstrate remarkable structural diversity and pharmacological versatility in the context of anti-inflammatory drug discovery. Systematic modification of these frameworks enables fine-tuning of potency, selectivity, and pharmacokinetic behavior, while hybridization and scaffold condensation strategies further support multi-target modulation of inflammatory and oxidative stress pathways. Collectively, these features highlight thiazole-based compounds as highly promising platforms for the development of next-generation anti-inflammatory agents with improved efficacy and safety profiles.

This strategic review systematizes the current data on the classification of thiazole compounds with anti-inflammatory activity, their mechanisms of action, as well as the results of preclinical studies *in vitro*. Special attention is paid to the prospects for optimizing molecules through multifunctional approaches, prodrug strategies and pharmacophore hybridization. The key challenges and promising directions for the development of potential anti-inflammatory agents based on the thiazole core are formulated, including the need for standardization of evaluation methods, implementation of computer modeling and artificial intelligence design. This review creates a scientific basis for the further development of thiazole anti-inflammatory agents and their integration into modern pharmacotherapy.

Funding

This publication was prepared as a result of the project No. 2025.07/0381 “Integrative design strategies for multifunctional bioactive substances based on uncondensed and condensed azoles and natural polyphenolic compounds”, funded by the National Research Foundation of Ukraine (NRFU).

Acknowledgement

The authors gratefully acknowledge the NRFU for supporting this research.

Conflicts of Interest

The authors declare no conflict of interest.

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