International Journal in Physical and Applied Sciences
Volume 11 Issue 07, Jully 2024 ISSN: 2394-5710 Impact Factor: 8.202
Journal Homepage: http://ijmr.net.in, Email: irjmss@gmail.com
Double-Blind Peer Reviewed Refereed Open Access International Journal

Biological Importance of Thiazolidinone

Dr Suneel Kumar

Assistant Professor

Department of Chemistry

Government Lohia College Churu Rajasthan

Abstract

Thiazolidinones are a prominent class of heterocyclic compounds characterized by a five-membered ring containing sulfur, nitrogen, and a carbonyl group. These molecules, particularly the 2- and 4-thiazolidinone derivatives, have been extensively investigated because of their wide spectrum of biological activities. Recent research highlights their potential as antimicrobial, anticancer, anti-inflammatory, antiviral, and antidiabetic agents. Their structural flexibility allows for extensive chemical modification, enabling structure–activity relationship (SAR) exploration and optimization of potency and selectivity. This article reviews the biological significance of thiazolidinone derivatives, summarizes recent literature, outlines objectives for continued study, and proposes a methodological framework for further investigation. The review also identifies challenges in pharmacokinetics and toxicity that must be resolved for these compounds to reach clinical application.

Keywords: thiazolidinone, heterocycles, pharmacology, antimicrobial, anticancer, enzyme inhibition

Introduction

Heterocycles form the backbone of many bioactive molecules, and among them thiazolidinones hold a special place. The presence of sulfur and nitrogen atoms in a compact five-membered ring system confers unique chemical and pharmacological properties. The carbonyl group further enhances their reactivity and binding potential to biological targets. Because of these features, thiazolidinones are considered “privileged scaffolds” in medicinal chemistry.

From a drug discovery standpoint, thiazolidinones are attractive due to three main factors. First, they possess drug-like physicochemical characteristics such as moderate polarity, suitable lipophilicity, and conformational rigidity. Second, they

can be synthesized through relatively simple reactions, allowing for rapid generation of structural analogues. Third, numerous studies have confirmed their diverse pharmacological profiles, spanning antimicrobial, anticancer, anti-inflammatory, antidiabetic, and antiviral domains.

Despite these advantages, only a limited number of thiazolidinone derivatives have progressed to advanced preclinical or clinical stages. This gap between laboratory findings and therapeutic development reflects challenges related to selectivity, pharmacokinetics, and long-term safety. The present review synthesizes available knowledge to highlight their biological potential, discuss structural trends, and propose directions for further research.

Review of Literature

Antimicrobial activity

Research has consistently shown that thiazolidinones possess broad-spectrum antimicrobial effects. Nefisath et al. (2024) synthesized 2,3,5-trisubstituted derivatives and reported strong antibacterial activity against Klebsiella pneumoniae

and notable antitubercular activity against Mycobacterium tuberculosis H37Rv. Docking studies suggested that these compounds interact with bacterial enzymes such as MurB and MPS. Similarly, Merlani and colleagues developed benzothiazole-thiazolidinone hybrids that demonstrated superior antibacterial and antifungal activity compared to standard antibiotics, with relatively low predicted toxicity.

Anticancer potential

Thiazolidinones have been investigated as inhibitors of oncogenic pathways. Eldaly et al. (2023) designed thiazolidinone-benzoate derivatives that inhibited epidermal growth factor receptor (EGFR), with some compounds showing nanomolar inhibitory concentrations. These molecules also induced apoptosis and caused cell cycle arrest in liver cancer cells, underscoring their promise as kinase-targeted anticancer agents. Furthermore, derivatives fused with natural product frameworks, such as dehydroabietic acid, exhibited potent activity against oral squamous

carcinoma, with computational models suggesting interactions with TLR4 and IGF1R.

Antidiabetic and metabolic applications

Khan et al. (2024) synthesized indole-oxadiazole linked thiazolidinones and observed inhibitory activity against α-glucosidase and α-amylase, enzymes crucial in carbohydrate metabolism. Docking analysis supported their binding to catalytic sites, making them candidates for managing postprandial hyperglycemia. These findings parallel the success of thiazolidinediones (a structurally related class) in diabetes therapy, though with potentially fewer adverse effects.

Anti-inflammatory and analgesic effects

Several thiazolidinone derivatives have been found to inhibit cyclooxygenase (COX) enzymes and reduce pro-inflammatory cytokines. Experimental models such as carrageenan-induced paw edema demonstrated significant anti-inflammatory activity. Hybridization with phenolic or heteroaryl motifs has been used to enhance antioxidant and radical-scavenging properties, suggesting a dual anti-inflammatory–antioxidant role.

Antiviral properties

Although less explored, certain thiazolidinones exhibit inhibitory activity against viral proteases and replication complexes. Docking studies propose that their carbonyl group and heteroaryl substituents allow interactions with active sites of viral enzymes. Further validation in cell culture and animal models is needed to confirm their potential as antiviral agents.

Gaps identified in literature

The majority of studies remain limited to in vitro assays and computational predictions.

Pharmacokinetic evaluation, such as absorption, distribution, metabolism, and excretion (ADME), is seldom reported.

Long-term safety and organ-specific toxicity require systematic evaluation.

In vivo efficacy studies are relatively scarce.

Objectives

The present research aims to:

1. Explore the biological importance of thiazolidinone derivatives through a critical review of recent studies.

2. Identify structure–activity relationships that govern antimicrobial, anticancer, anti-inflammatory, and antidiabetic activity.

3. Propose a methodological framework for designing and evaluating new thiazolidinone derivatives.

4. Highlight challenges related to pharmacokinetics, toxicity, and clinical translation.

5. Suggest future directions for developing thiazolidinone-based therapeutic agents

Research Methodology

Since this work is primarily a review with a proposed framework, the methodology involves two major components:

1**. Literature Review**

Comprehensive search of peer-reviewed journals and databases (PubMed, Scopus, Web of Science, ScienceDirect).

Selection of articles published mainly in the last ten years (2015–2025), with emphasis on experimental studies and SAR analyses.

Inclusion criteria: original synthesis of thiazolidinone derivatives, biological activity evaluation, computational modeling, and pharmacokinetic/toxicity studies.

Exclusion criteria: patents without experimental data, non-peer reviewed reports, and studies lacking clear methodology.

2. **Proposed Experimental Framework for Future Work**

Design and synthesis: Utilize multicomponent reactions to generate substituted thiazolidinones, focusing on C-2 and C-5 substitutions.

Characterization: Confirm structures via spectroscopy (NMR, IR, MS) and possibly crystallography.

Biological assays: Antimicrobial: MIC determination against Gram-positive, Gram-negative, and fungal species.

Anticancer: Cytotoxicity assays on cancer and normal cell lines, apoptosis assays, and cell cycle studies.

Enzyme inhibition: α-glucosidase, α-amylase, and COX enzymes.

In silico studies: Docking and dynamics simulations to identify binding modes with target proteins.

Pharmacokinetic screening: Predict solubility, logP, bioavailability, and toxicity using computational tools; validate experimentally where possible.

Biological Activities and Mechanisms

Antimicrobial Action

Thiazolidinones may disrupt bacterial enzyme systems such as DNA gyrase, MurB reductase, or dihydrofolate reductase. The lipophilicity of aryl substituents facilitates membrane penetration, while polar groups enhance solubility and reduce host toxicity.

Anticancer Mechanisms

Reported mechanisms include inhibition of kinases (e.g., EGFR), induction of apoptosis via caspase activation, disruption of tubulin polymerization, and generation of reactive oxygen species that selectively damage cancer cells.

Anti-inflammatory Pathways

Compounds reduce nitric oxide production and inhibit NF-κB signaling. Substitution with electron-donating groups at the phenyl ring often enhances anti-inflammatory potency.

Antidiabetic Effects

By inhibiting α-glucosidase and α-amylase, thiazolidinones delay carbohydrate digestion and glucose absorption, improving glycemic control.

Structure–Activity Relationship (SAR) Insights

N-Substitution: Alters lipophilicity; bulky groups often enhance cell penetration.

C-2 and C-5 substituents: Halogens and nitro groups frequently enhance antimicrobial and anticancer activity.

Hybrid molecules: Linking thiazolidinones with other active scaffolds (indole, quinoline, benzothiazole) often yields compounds with dual or synergistic effects.

Challenges in Development

1. **Selectivity:** Some compounds display broad activity that risks off-target effects.

2. **Pharmacokinetics**: Poor solubility and rapid metabolism are common hurdles.

3. **Toxicity:** Long-term safety profiles are insufficiently studied.

4. **Clinical translation:** Few compounds have advanced beyond preclinical models.

Future Directions

Utilize structure-based drug design and computational screening to improve selectivity.

Explore nanocarrier or prodrug formulations to overcome solubility and bioavailability issues.

Conduct systematic in vivo studies for efficacy and toxicity.

Develop multitarget thiazolidinone hybrids for complex diseases such as cancer and neurodegeneration.

Conclusion

Thiazolidinones represent a versatile heterocyclic framework with wide-ranging biological importance. Studies highlight their promise as antimicrobial, anticancer, anti-inflammatory, antidiabetic, and antiviral agents. However, challenges in pharmacokinetics, toxicity, and translational research remain. With continued SAR exploration, hybrid molecule design, and robust pharmacological evaluation, thiazolidinones hold potential as lead scaffolds for future therapeutic development.

References

1. Nefisath, P., Vasantha Kumar, S., Shashiprabha, et al. (2024). 2,3,5-Trisubstituted Thiazolidinone Derivatives as Potential Antimicrobial and Antitubercular Agents. ChemistrySelect.

2. Eldaly, M., et al. (2023). Design, Synthesis, and Anticancer Evaluation of New Thiazolidinone-Benzoate Scaffold as EGFR Inhibitors. Chemistry & Biodiversity.

3. Khan, S., Hussain, R., et al. (2024). Hybrid Indole-Oxadiazole Linked Thiazolidinone Derivatives as Potential Antidiabetic Agents. Pharmaceuticals, 17(11), 1428.

4. Merlani, M., Barbakadze, V., et al. (2019). Benzothiazole-Based Thiazolidinones as Antimicrobial Agents: Design and Biological Evaluation. Bioorganic & Medicinal Chemistry.

5. Seboletswe, K., et al. (2023). Thiazolidinone-Heterocycle Frameworks: Pharmacological Significance. ChemMedChem.

6. Drzał, W., Trotsko, N. (2021). Advances in Thiazolidin-4-One Derivatives as Antitubercular Agents. Molecules, 30(10), 2201.

7. MDPI Review (2022). 4-Thiazolidinone Bearing Hybrid Molecules in Anticancer Drug Design. International Journal of Molecular Sciences, 23(21), 13135.

8. Abhinit, K., & Singh, A. (2020). Thiazolidinones: A Review on Synthesis, Reactions, and Biological Importance. Journal of Heterocyclic Chemistry, 57(2), 534–552.

9. Varghese, B., Al-Busafi, S., et al. (2017). Thiazolidinone Derivatives: Synthesis, Reactions and Biological Activity. Arabian Journal of Chemistry, 10(S2), S2741–S2761.

10. Bansal, R., et al. (2018). Molecular Docking and SAR Study of Thiazolidinone Derivatives as Anticancer Agents. European Journal of Medicinal Chemistry, 156, 480–495.

11. Nascimento, T. L., et al. (2019). Antimicrobial and Antioxidant Activities of Thiazolidinone Derivatives. Frontiers in Chemistry, 7, 684.

12. Rashid, U., et al. (2019). Synthesis and Biological Evaluation of Novel Thiazolidinones as Potential Antidiabetic Agents. Bioorganic Chemistry, 89, 103022.

13. Abdel-Aziz, H. A., et al. (2016). Anti-inflammatory and Analgesic Evaluation of Novel Thiazolidinone Derivatives. European Journal of Pharmacology, 791, 626–634.

14. Rani, N., & Kumar, R. (2021). Role of Thiazolidinone Derivatives in Drug Discovery. Mini-Reviews in Medicinal Chemistry, 21(5), 652–665.

15. Mohareb, R. M., et al. (2020). Thiazolidinone Hybrids as Promising Therapeutics: Design, Synthesis, and Biological Evaluation. Archiv der Pharmazie, 353(9), e2000096.