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A Literature Survey on Biological Activities of Thiazolidine Derivatives

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Abstract

Thiazolidine derivatives are the significant class of heterocyclic compounds known for their broad biological activities. These include antimicrobial, anticancer, anti-inflammatory, antidiabetic, antiprotozoal, antioxidant, and antitubercular effects. Among them, 4-thiazolidinones are particularly notable due to their pharmacological versatility. Recent research has focused on synthesizing novel derivatives, especially thiadiazole-linked compounds, showing promising activity against drug-resistant Mycobacterium tuberculosis. Their structural diversity and ability to target multiple pathways make them valuable in drug discovery. This review highlights recent developments and the therapeutic potential of thiazolidine-based molecules The importance of thiazolidine derivatives lies in their ability to serve as privileged scaffolds for drug design. Structural modifications on the thiazolidine ring can lead to profound changes in biological response, making these compounds attractive for medicinal chemists. For instance, substitutions at the 2, 3, or 5 positions of the thiazolidine nucleus often result in enhanced selectivity and potency. Furthermore, the ease of synthesizing thiazolidine derivatives through cyclization reactions involving primary amines and thioglycolic acid provides a convenient pathway for generating libraries of analogs for biological screening. In the field of antimicrobial drug development, 4-thiazolidinones have emerged as potential agents against both Gram-positive and Gram-negative bacteria. Several studies have shown that thiazolidine derivatives can act on bacterial cell wall synthesis or interfere with essential enzymatic functions, thereby offering new leads in the era of antibiotic resistance. Similarly, their role in anticancer therapy has been increasingly documented, with some derivatives demonstrating the ability to inhibit tumor growth by inducing apoptosis or blocking signaling pathways such as PI3K/Akt and MAPK Another notable application is in the treatment of diabetes mellitus, where thiazolidinediones—a subclass of thiazolidine derivatives—have been successfully used as insulin sensitizers. These compounds act by binding to peroxisome proliferator-activated receptor gamma (PPAR-γ), improving glucose metabolism and reducing insulin resistance. Although their use has been limited due to side effects, they remain an important example of how thiazolidine derivatives can be translated into clinically useful drugs. In the context of tuberculosis, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains has intensified the search for new chemical entities. Thiazolidinone–thiadiazole hybrids have attracted attention for their ability to inhibit key enzymes of M. tuberculosis and disrupt cell wall integrity. These hybrid molecules combine two bioactive moieties, thereby enhancing their pharmacological profile and reducing the likelihood of resistance development. Overall, thiazolidine derivatives represent a versatile platform for drug discovery. Their wide range of biological activities, structural flexibility, and synthetic accessibility ensure that they will continue to play a central role in medicinal chemistry research. Future investigations aimed at improving their pharmacokinetics, reducing toxicity, and

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exploring novel targets may lead to the development of next-generation therapeutics derived from this fascinating heterocyclic system.

Keywords: Antimicrobial drug, tuberculosis, thiazolidine, biological activities, heterocyclic compounds

INTRODUCTION

Heterocyclic compounds play a vital role in both chemical and life sciences. Among them, thiazolidinones represent a significant class, characterized by a five-membered saturated ring containing both sulfur and nitrogen atoms. Structurally, thiazolidinones are derived from thiazole, with the sulfur position at the 1-position, nitrogen at the 3-position, and a carbonyl group typically located at the 2-, 4-, or 5- positions, although structural and functional diversity is most strongly influenced by the group attached at the 2-position carbon 4- Thiazolidinones, in particular, derivatives of thiazolidine featuring a carbonyl group in thiazolidinones are generally unreactive, and its interaction with Lawesson's reagent can yield the corresponding 4-thione derivatives. The presence of heteroatoms, such as nitrogen, sulfur, and oxygen, contributes to the broad biological activity of many heterocyclic compounds.

Notably, 4-thiazolidinone is a pharmacophore of significant interest owing to its wide spectrum of biological activities. These include anti-inflammatory, analgesic, antimicrobial, antiproliferative, antiviral, anticonvulsant, antidiabetic, antihyperlipidemic, cardiovascular, antitubercular, antifungal, antibacterial, and antitumor effects across various cancer cell lines, such as leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate, and breast cancers. Thiazolidinones undergo diverse chemical transformations and serve as precursors to other heterocyclic systems such as thiazoles, benzimidazoles, thiopyrano-thiazolones, benzodiazepines, triazoles and benzothiophenes [1].

ANTIMALARIAL ACTIVITY

Solomon et al. synthesized a series of chloroquine analogs incorporating a 1,3-thiazolidine-4-one moiety at the terminal amino group of the 4-aminoquinoline structure (compound XVI). These compounds were tested for their antimalarial efficacy against *P. falciparum* in vitro. Among them, several demonstrated activities on par with the standard antimalarial drug and were further tested in vivo against *Plasmodium yoelii* (Figure 1). The most effective compound exhibited an IC50 value of 0.039 μM, which was significantly higher than that of chloroquine [2].

ANTICANCER ACTIVITY

In a separate study, Gududuru et al. synthesized a series of 2-amyl- 40oxothiazolidin-3-yl amides, which were evaluated for their ability to inhibit prostate cancer cell growth. Several potent compounds have been identified, demonstrating improved selectivity in killing prostate cancer cells compared to serine amide phosphates. Among these, the compound was found to be the most effective (Figure 2). The study revealed that substitution of a nitrogen atom with a long alkyl chain led to increased anticancer activity [3–6].

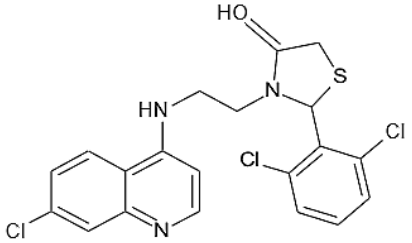


Figure 1. 2-(2-chloro-6-methylphenyl)-3-{2-[(7-chloroquinolin-4-yl)amino]ethyl}-1,3-thiazolidin-4-one.

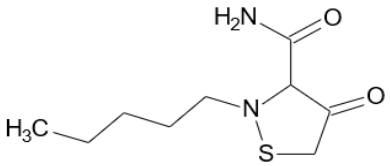


Figure 2. 4-oxo-2-pentyl-1,2-thiazolidine-3-carboxamide.

ANTIOXIDANT ACTIVITY

Shih et al. developed a series of sydnonyl-substituted thiazolidinone and thiazoline derivatives that were subsequently assessed for their antioxidant properties. Among these, this compound demonstrated notable 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity. Its antioxidant potential was comparable to that of vitamin E, indicating its significant free radical neutralization capability (Figure 3) [2].

ANTI-INFLAMMATORY ACTIVITY

Novel 5-arylidene-2-(1,3-thiazol-2-ylimino)-1,3-thiazolidin-4-ones were synthesized and evaluated for their dual anti-inflammatory and antimicrobial activities by Apostolidis et al. Among the tested compounds, compound 1 exhibited the most potent lipoxygenase (LOX) inhibitory activity, whereas compound 2 demonstrated the highest anti-inflammatory effect, including 50% inhibition of cyclooxygenase-1(COX-1) (Figure 4) [1].

ANTIPROTOZOAL ACTIVITY

Shafiee Yazdikarimy et al. designed and synthesized 1-methyl-2-(1,3,4- thiadiazole-2-yl)-5-nitroimidazole and 1-methyl-2-(1,3,4-oxadiazole-2-yl)-5- nitroimidazole compounds with the aim of exploring their potential as antiprotozoal agents (Figure 5) [7–10].

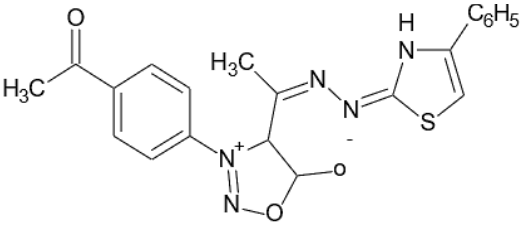
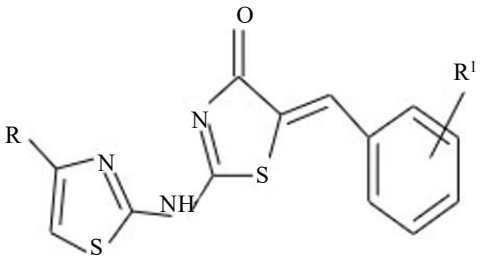


Figure 3. Sydnonyl-substituted thiazolidinone and thiazoline derivatives.



Compound 1	Compound 2
R=H	R=H
R1=2,5-diOCH$_3$	R1=N(CH$_3$)$_2$

Figure 4. Inhibition of cyclooxygenase-1(COX-1).

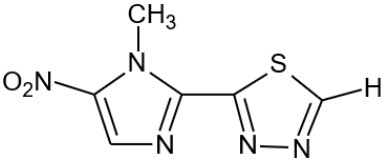


Figure 5. 2-(1-methyl-5-nitro-1H-imidazol-2-yl)-1,3,4-thiadiazole.

ANTIDIABETIC ACTIVITY

Thiazolidinediones (TZDs) are a well-known class of antidiabetic drugs that function as insulin sensitizers by activating peroxisome proliferator-activated receptor-Y(PPAR-Y). Several TZDs are commercially available.

Antidiabetic activity refers to the ability of a compound, plant extract, or drug to lower blood glucose levels and improve the management of diabetes mellitus, a metabolic disorder characterized by chronic hyperglycemia. Diabetes occurs because of either insufficient insulin secretion (type 1 diabetes) or impaired insulin action and resistance (type 2 diabetes). Antidiabetic agents aim to restore glucose homeostasis, prevent complications, and improve overall quality of life.

Conventional antidiabetic drugs include insulin, sulfonylureas, biguanides (such as metformin), thiazolidinediones, α-glucosidase inhibitors, and newer classes such as DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors. They act through different mechanisms, such as stimulating insulin release, improving insulin sensitivity, reducing glucose absorption from the intestine, and promoting renal glucose excretion.

In 2016, Datar and colleagues synthesized a new series of thiazolidine-3-yl acetic acid derivatives. These compounds were evaluated for their hypoglycemic (blood sugar-lowering) activity using an in vivo sucrose-loaded model in Wistar rats (Figure 6) [6].

ANTITUBERCULAR ACTIVITY

Tuberculosis (TB), which is caused by *Mycobacterium tuberculosis*, remains a serious global health concern. The treatment of TB is becoming increasingly challenging due to the emergence of mono-drug and multi-drug-resistant (MDR) strains of *M. tuberculosis*. There is an urgent need for the development of new drugs with novel chemical structures.

Antitubercular activity refers to the ability of a synthetic or natural substance to inhibit the growth of *Mycobacterium tuberculosis*, the causative agent of tuberculosis (TB). TB remains a major global health concern, especially in developing countries, owing to its high morbidity, mortality, and increased drug resistance. Effective antitubercular agents are essential for the control and eradication of TB.

Standard first-line antitubercular drugs include isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin. These agents target vital bacterial processes such as cell wall synthesis, RNA transcription, or energy metabolism. Their combined use reduces the risk of resistance and shortens treatment duration. However, the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) poses significant challenges, making the search for new molecules with potent antitubercular activity critical.

Research efforts have explored diverse chemical classes, such as quinolones, oxazolidinones, and nitroimidazoles, as well as natural products from plants, fungi, and marine sources. These potential candidates were screened using in vitro and in vivo models of *M. tuberculosis* strains. In addition to novel agents, repurposing of existing drugs with known safety profiles is gaining attention.

Assessment of antitubercular activity involves determining the minimum inhibitory concentration (MIC), bactericidal effects, and efficacy against resistant strains. Advances in molecular biology and

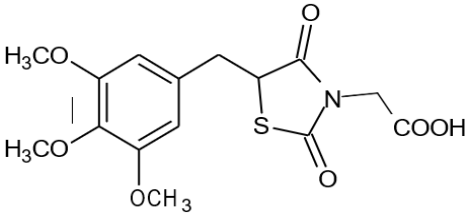


Figure 6. 22.84% blood glucose level decreased by AUC method.

computational drug design have accelerated the identification of promising therapeutic leads. Ultimately, enhancing antitubercular activity through new drugs, combination therapies, and innovative delivery systems is crucial for overcoming drug resistance and achieving global TB control.

Over the past decade, the research for new antitubercular agents has become a priority in chemotherapeutics research. Among various chemical classes investigated, thiadiazole derivatives have garnered significant attention due to their promising biological activity against *Mycobacterium tuberculosis*.

The aim of the present study was to explore and develop novel molecules with enhanced potential for tuberculosis treatment. In this context, a series of N-phenyl-N-[4-(5-alkyl/arylamino-1,3,4-thiadiazole-2-yl)phenyl]thiourea derivatives (compounds) was synthesized by Karakus et al. in 2004. The antitubercular activity of the synthesized compounds was evaluated in vitro using the BACTEC 460 Radiometric System against *Mycobacterium tuberculosis* H37Rv at a concentration of 6.25μg/ml (Figure 7) [5].

ANTITUMOR ACTIVITY

Dasatinib represents a major advancement in the treatment of chronic myeloid leukemia, especially in patients who are resistant to imatinib therapy. It functions as a dual inhibitor of BCR-ABL and Src family kinases, effectively targeting both the wild-type and mutant forms of BCR-ABL. Its pharmacokinetic profile indicated a half-life of 3–5 h and an oral clearance rate of 363.8 L/hr.

Mechanistically, dasatinib binds to both the active and inactive conformations of the ABL kinase domain, enabling more effective inhibition than first-generation inhibitors. With a high binding affinity (Ki=0.5nM), it exhibits potent activity against 14 out of 15 known imatinib resistant BCR-ABL mutations (Figure 8) [4].

CONCLUSION

Thiazolidine derivatives, particularly thiazolidinones, have a broad spectrum of biological activities, making them promising candidates for drug discovery. Their structural versatility enables interactions with multiple biological targets, contributing to their efficacy in treating various diseases including cancer, diabetes, infections, and tuberculosis. Recent studies have shown significant progress in the development of derivatives with enhanced potencies and selectivity. Compounds with antitubercular and anticancer potential are particularly notable. Further research and structural optimization may lead

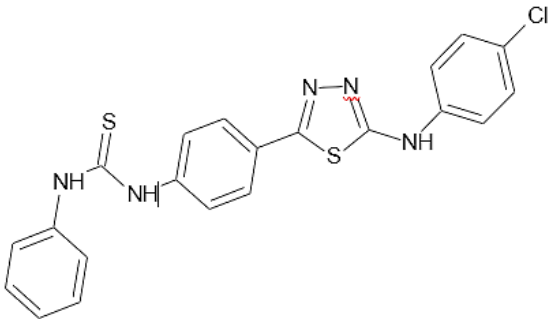


Figure 7. *N*-{4-[5-(4-chloroanilino)-1,3,4-thiadiazol-2-yl]phenyl}-*N*'-phenylthiourea.

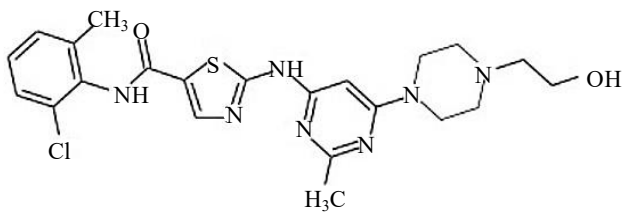


Figure 8. Structure of dasatinib.

to the development of novel therapeutics. Thus, thiazolidine derivatives hold great promise for modern medicinal chemistry.

REFERENCES

1. Kapoor G, Pathak DP, Bhutani R, Kant R. Thiazolidinone as a pharmacologically active molecule. J Chem Pharm Res. 2016;8:151–168.
2. Pandey YP, Singh AS, Sharma PKS, Kumar NK. Biological activities of thiazolidine – a review. J Curr Pharm Res. 2011;1:192–196. doi:10.33786/JCPR.2011.v01i02.018.
3. Singh TP, Sharma PK, Kaur PK, Mondal SC, Gupta A. Pharmacological evaluation of thiazolidinone derivatives: a perspective review. Pharma Chemica. 2011;3:194–206.
4. Kanchumarthy SJ, Rasajna G, Kamala G, Nehitha P, Deepthi P, Madhavi K, Likitha G, Narendra P. Current advances in synthesis and therapeutic applications of thiazole and its derivatives. J Pharma Insights Res. 2024;2:107–114. doi:10.69613/4ph6pj28.
5. Mishra G, Jyoti K. Review on biological activities of 1,3,4-thiadiazole derivatives. J Appl Pharm Sci. 2011;1:44–49.
6. Jain A, Kumar Sahu SK. Thiazolidine derivatives and their pharmacological actions. In: E3S Web Conf. Les Ulis (France): EDP Sciences; 2024. Vol. 556:01052. doi:10.1051/e3sconf/202455601052.
7. Kempegowda SK, Kumar DP, TM. Thiadiazoles: progress report on biological activities. Pharma Chemica. 2011;3:330–341.
8. Pandey Y, Sharma PK, Kumar N, Singh A. Biological activities of thiazolidine: a review. Int J PharmTech Res. 2011;3(2):980–985.
9. Jain AK, Vaidya A, Ravichandran V, Kashaw SK, Agrawal RK. Recent developments and biological activities of thiazolidinone derivatives: a review. Bioorg Med Chem. 2012;20:3378–3395. doi:10.1016/j.bmc.2012.03.069.
10. Singh SP, Parmar SS, Raman K, Stenberg VI. Chemistry and biological activity of thiazolidinones. Chem Rev. 1981;81:175–203. doi:10.1021/cr00042a003.

