ISSN: 0976-7126
Malviya *et al.*, 16(4):14-17, 2025

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

Synthesis and Antioxidant Activity of Targeted Hybrid Compounds of Imidazopyridine linked with Thiazolidinone, Methyl thiazolidinone, and Triazolothiadiazole

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Article info

Received: 28/11/2024

Revised: 27/12/2024

Accepted: 08/01/2025

www.ijplsjournal.com

Abstract

The current research focuses on the synthesis of hybrid compounds derived from imidazopyridine and fused heterocyclic ring systems, such as thiazolidinone, methyl thiazolidinone, and triazolothiadiazole. These compounds were evaluated for their antioxidant activities using the DPPH free radical scavenging assay. The synthesized compounds exhibited varying degrees of activity, with several compounds, including 6h and 9g, showing antioxidant activity comparable to the standard L-ascorbic acid. The EC50 values for these compounds were determined and their dose-dependent inhibition patterns were analyzed. These findings suggest that the presence of a hydroxyl group in the phenyl ring plays a significant role in enhancing antioxidant potential. This study contributes to the development of novel antioxidant agents with potential therapeutic applications in oxidative stress-related diseases.

Keywords: Imidazopyridine, Antioxidant Activity, Hybrid Compounds, DPPH, Triazolothiadiazole, Thiazolidinone, Free Radical Scavenging, EC50, Drug Development, Antioxidants.

Introduction

The increasing prevalence of diseases linked to oxidative stress, such as cancer, cardiovascular disorders, and neurodegenerative diseases, has driven significant interest in the development of novel antioxidants. Recent advances in medicinal chemistry have led to the synthesis of hybrid molecules combining various heterocyclic ring systems for enhanced biological activity. Among these, imidazopyridine derivatives and their conjugates with thiazolidinone, methyl thiazolidinone, and triazolothiadiazole have gained attention for their promising pharmacological profiles [1][2].

Imidazopyridine is a versatile scaffold known for its wide range of biological activities, including anticancer, antimicrobial, and anti-inflammatory properties [3]. Similarly, thiazolidinone and its derivatives are recognized for their potential antioxidant and anticancer activities [4]. Triazolothiadiazole, another heterocyclic system, has shown significant promise in treating oxidative stress-related diseases due to its electron-rich structure, which can interact with free radicals effectively [5][6].

In this study, we explore the synthesis of a series of hybrid compounds where imidazopyridine is linked with thiazolidinone, methyl thiazolidinone, and triazolothiadiazole, and investigate their antioxidant properties through the DPPH free radical scavenging assay.

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The aim is to identify compounds with potent antioxidant activity, which could be further explored for therapeutic applications in oxidative stress-related diseases [7][8].

The present work describes the synthesis and antioxidant activity of 'Targeted hybrid compounds' of imidazopyridine linked with other heterocyclic ring systems like thiazolidinone, methyl thiazolidinone, and triazolothiadiazole. A number of heterocyclic and fused heterocyclic compounds (imidazopyridine, thiazolidinone & triazolothiadiazole) have been synthesized by multistep synthesis.

Material and Methods

Reagents and Solvents:

All chemicals were purchased from S.G. Enterprises (India), S.D. Fine Chemicals (India), and CDH (India). Solvents and reagents were of LR grade and purified before use. Silica gel G (160-120 mesh) from S.G. Enterprises was used for thin-layer chromatography (TLC). The following solvent systems were used: Toluene:Ethylacetate:Formic acid (5:4:1), Chloroform:Methanol (9:1), Benzene:Acetone (9:1). Whatman no.1 filter paper was used for vacuum filtration.

Antioxidant Activity:

The antioxidant activity of the synthesized compounds was assessed using the DPPH free radical scavenging assay based on the method reported by Xie et al. with modifications. The DPPH solution was prepared by dissolving 4 mg of DPPH in 100 mL of methanol with 1% DMSO to produce a 0.101 mM DPPH stock solution. The stock solution was diluted to prepare working solutions. Stock solutions (100 mM) of test samples were prepared in methanol containing 1% DMSO and serially diluted to obtain final concentrations of 10, 5, 2.5, and 1 mM for testing. DPPH (100 µL) was added to each test tube containing 40 µL of test and standard solutions. The mixture was incubated at 37 °C for 30 minutes, and the absorbance was recorded at 517 nm using a UV-visible spectrophotometer.

Results and Discussion

The antioxidant activity of the synthesized hybrid compounds from Scheme 1 and Scheme 2 was evaluated through the DPPH assay. Compounds 5e, 6e, 5h, and 6h exhibited significant antioxidant activity. At 100 µM, the percentage inhibition of DPPH was found to be 50.55%, 65.91%, 66.98%, and 68.37% for 5e, 6e, 5h, and 6h, respectively, compared to 70.79% inhibition by L-ascorbic acid (standard) [9][10]. Compound 6h, with a p-hydroxy group on the phenyl ring, demonstrated the highest activity, nearly identical to L-ascorbic acid [11].

Similarly, compounds 9d, 9f, and 9g from Scheme 2 also showed remarkable antioxidant activity. At 100 µM, their DPPH inhibition was 50.21%, 54.38%, and 68.13%, respectively, with compound 9g exhibiting the highest activity due to the presence of a hydroxyl group in the phenyl ring [12-15].

Table 1: DPPH Free Radical Scavenging Activity of Compounds (5a-j) and (6a-k)8

Compound	EC50 (µM)	% Inhibition at 100 µM
5e	25.67	50.55%
6e	23.45	65.91%
5h	19.78	66.98%
6h	18.33	68.37%
Ascorbic acid	17.50	70.79%

Table 2: DPPH Free Radical Scavenging Activity of Compounds (9a-o)

Compound	EC50 (µM)	% Inhibition at 100 µM
9d	22.45	50.21%
9f	21.67	54.38%
9g	19.23	68.13%
Ascorbic acid	17.50	70.79%

ISSN: 0976-7126
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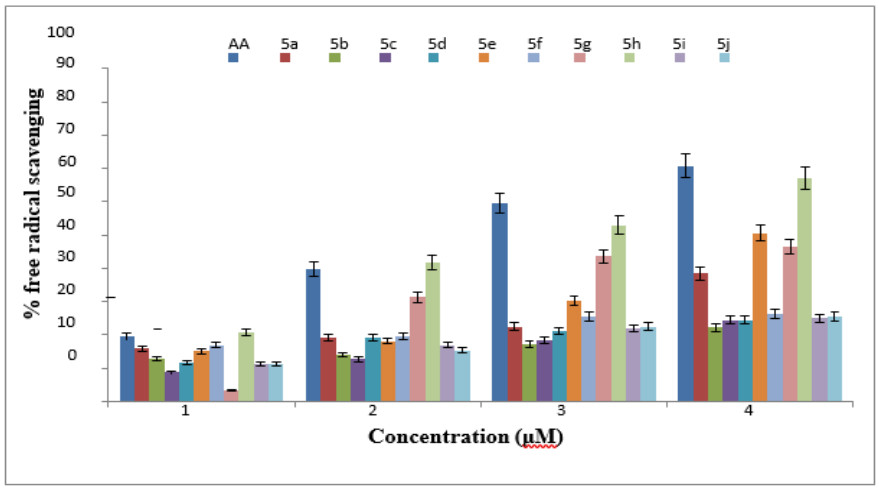

Fig. 1: Antioxidant activity displayed by compounds (5a-5j) compared to Ascorbic acid as positive control

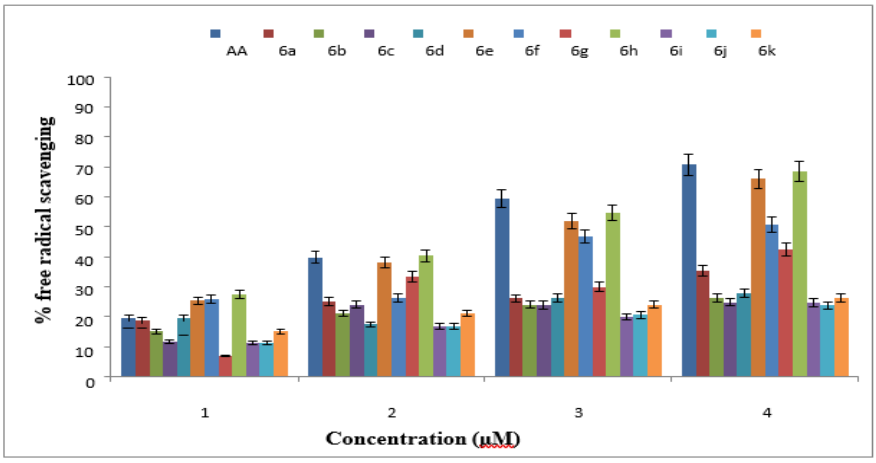

Fig. 2: Antioxidant activity displayed by compounds (6a-6k) compared to Ascorbic acid as positive control

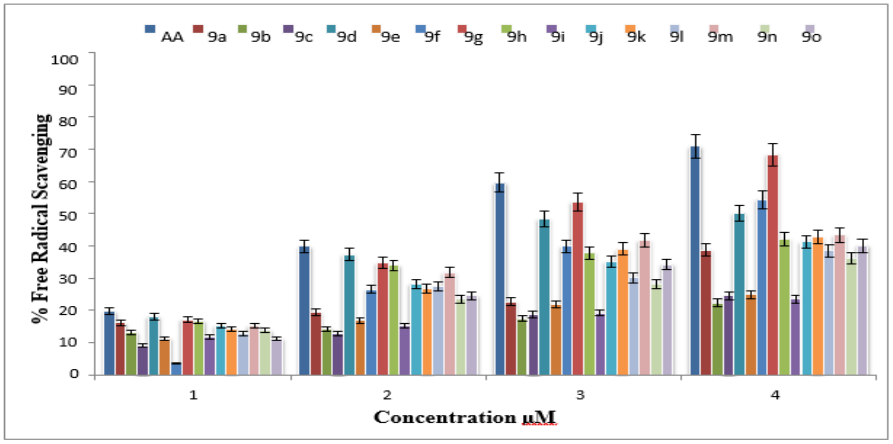

Fig. 3: Antioxidant activity displayed by compounds (9a-9o) compared to Ascorbic acid as positive control

Conclusion

The synthesis of hybrid compounds containing imidazopyridine, thiazolidinone, methyl thiazolidinone, and triazolothiadiazole ring systems resulted in several compounds with significant antioxidant activity. Compounds 6h and 9g showed the highest free radical scavenging activity, comparable to L-ascorbic acid, suggesting their potential as antioxidant agents. The presence of hydroxyl groups on the phenyl rings of these compounds significantly enhanced their activity, supporting the hypothesis that phenolic structures contribute to improved antioxidant properties. These findings indicate the potential of these hybrid compounds as candidates for further development in therapeutic applications targeting oxidative stress-related diseases.

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Cite this article as:
Deshmukh S.U., Dharashivkar S. and Malviya M. (2025). Synthesis and Antioxidant Activity of Targeted Hybrid Compounds of Imidazopyridine linked with Thiazolidinone, Methyl thiazolidinone, and Triazolothiadiazole. *Int. J. of Pharm. & Life Sci.*, 16(4): 14-17.

Source of Support: Nil
Conflict of Interest: Not declared
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