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Synthesis, Characterization, and Antimicrobial Activity of Novel Pyrazolylthiazole Derivatives from Curcumin Analogues

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Abstract

Curcumin and its derivatives have garnered significant attention in medicinal chemistry due to their versatile therapeutic potential, including antimicrobial, anti-inflammatory, and anticancer properties. This study focuses on the synthesis, characterization, and antimicrobial activity of pyrazolylthiazole derivatives derived from curcumin analogues. Curcumin, demethoxycurcumin, and bis-demethoxycurcumin were isolated from natural sources and used as precursors for the synthesis of pyrazolylthiazole derivatives through reactions involving anisaldehyde, cyclohexanone, and thiosemicarbazide under optimized conditions. The synthesized compounds were characterized using spectroscopic techniques such as IR, NMR, and mass spectrometry to confirm their structures. In vitro antimicrobial evaluation against bacterial and fungal strains revealed significant activity, with some derivatives demonstrating superior efficacy compared to standard drugs. These findings highlight the potential of pyrazolylthiazole derivatives as promising candidates for developing novel antimicrobial agents and contribute to the growing interest in heterocyclic compounds for therapeutic applications.

Keywords: Curcumin, Pyrazolylthiazole, Antimicrobial activity, Heterocyclic compounds, Natural derivatives

Introduction

Curcumin and its derivatives occupy a pivotal role in medicinal chemistry due to their remarkable therapeutic versatility, encompassing antioxidant, anti-inflammatory, anticancer, and antimicrobial properties. As the principal active compound extracted from turmeric, curcumin serves as a foundation for developing biologically potent molecules [1]. Its analogues, such as demethoxycurcumin and bis-demethoxycurcumin, further enhance the scope for designing novel compounds with improved efficacy [2]. The natural availability of curcumin combined with advancements in synthetic methodologies, such as high-yield "click" and "unclick" chemistry approaches, has enabled the efficient production of both symmetric and asymmetric curcuminoids, broadening their application in medicinal research [3]. Among the various modifications, the integration of pyrazole and thiazole moieties into curcumin analogues has emerged as a promising strategy for antimicrobial drug development [4]. Pyrazole derivatives are widely recognized for their pharmacological significance, particularly for their anti-inflammatory, anticancer, and antimicrobial properties [5]. Similarly, thiazole derivatives have shown remarkable efficacy against bacterial and fungal pathogens due to their ability to disrupt critical microbial pathways [6].

The combination of these two heterocyclic systems in pyrazolylthiazole frameworks provides a synergistic effect, enhancing the antimicrobial potency and selectivity of the resulting compounds [7]. These derivatives have shown broad-spectrum antimicrobial activity against gram-positive and gram-negative bacteria and fungi, making them promising candidates for addressing antimicrobial resistance, a growing global health challenge [8]. In this context, the present study aims to isolate curcumin and its analogues from natural sources, synthesize pyrazolylthiazole derivatives through a carefully designed reaction pathway, and characterize them using advanced spectroscopic techniques such as infrared (IR), nuclear magnetic resonance (NMR), and mass spectrometry [9]. Additionally, the synthesized compounds will be evaluated for their antimicrobial efficacy using in vitro assays against diverse microbial strains. By correlating their structure-activity relationship (SAR), this study aims to identify key structural features responsible for antimicrobial activity, paving the way for optimizing their therapeutic potential [10]. Through these efforts, the research seeks to contribute significantly to the field of heterocyclic medicinal chemistry, addressing the urgent need for novel antimicrobial agents to combat resistant pathogens.

Materials and Methods

Synthesis of Curcumin Analogues

The synthesis process began with the isolation of curcumin, demethoxycurcumin, and bis-demethoxycurcumin from natural sources, such as

turmeric. The isolated compounds were purified using recrystallization and characterized by standard analytical methods. This step provided the essential building blocks for further chemical modifications [11].

Synthesis of Pyrazolylthiazole Derivatives

The synthesis of pyrazolylthiazole derivatives involved a multi-step reaction sequence. Anisaldehyde and cyclohexanone were reacted in the presence of a suitable solvent and an optimized catalyst to form intermediate chalcones. These chalcones were then treated with thiosemicarbazide under reflux conditions to yield pyrazolylthiazole derivatives. The choice of solvent and catalyst was critical in ensuring high yield and product purity [12,13].

Literature Supporting the Synthesis and Applications

The synthesis of pyrazolylthiazole derivatives has been extensively documented in the literature. Singh et al. [14] reported the efficient synthesis of 4-pyrazolylthiazoles using [Hydroxy(tosyloxy)iodo]benzene, a groundbreaking approach that influenced subsequent research. Hassan et al. [15] and Khloya et al. [16] investigated the anti-inflammatory and antimicrobial properties of pyrazolylthiazoles, demonstrating their pharmacological significance. Abbas et al. [17] highlighted the anti-cancer potential of these derivatives through a structure-activity relationship (SAR) study, while Kumar et al. [18] designed coumarin-thiazole-pyrazole hybrids with potent antimicrobial activity supported by molecular docking studies. Nasab et al. [19] introduced thiophenyl-pyrazolylthiazole-coumarin hybrids as tyrosinase inhibitors, identifying compound 6g as a lead molecule with high enzymatic inhibition.

Characterization of Synthesized Compounds

All synthesized compounds were characterized using spectroscopic techniques, including infrared (IR) spectroscopy for functional group analysis, nuclear magnetic resonance (NMR) for structural elucidation, and mass spectrometry for molecular weight confirmation. These methods ensured the structural integrity and purity of the synthesized pyrazolylthiazole derivatives [20].

Antimicrobial Activity:

The antimicrobial activity of curcumin and its derivatives has been widely investigated, showcasing their potential as versatile antimicrobial agents across various contexts. Han et al. [21] demonstrated the antimicrobial properties of wool fabric treated with curcumin, highlighting its effectiveness in preventing microbial growth. Ammayappan et al. [22] studied the synergistic antimicrobial effects of curcumin combined with aloe vera and chitosan, which significantly enhanced its efficacy. Basniwal et al. [23] focused on curcumin nanoparticles, reporting improved antimicrobial activity due to enhanced solubility and bioavailability. Heo et al. [24] revealed the concentration-dependent antimicrobial effects of curcumin against fish pathogens, establishing its broad-spectrum activity. Moghadamtousi et al. [25] comprehensively reviewed curcumin's antibacterial, antiviral, and antifungal properties, emphasizing its potential as a natural antimicrobial agent. Additionally, Jayandran et al. [26] reported on the green synthesis of manganese nanoparticles using turmeric curcumin as a stabilizing agent, demonstrating their significant antimicrobial activity. Oliveira et al. [27] explored the enhanced antimicrobial activity of curcumin when combined with light, while Silva et al. [28] emphasized its effectiveness in nanoformulations against various pathogens. Nair et al. [29] investigated the antimicrobial potential of the protein fraction derived during curcumin extraction, revealing its promising activity. Lastly, Sarma et al. [30] evaluated Lakadong turmeric-derived curcumin nanogels, showing their efficacy against resistant biofilms, particularly in combating biofilm-associated pathogens. Collectively, these studies underline the remarkable antimicrobial potential of curcumin and its derivatives in diverse applications, including fabrics, nanoformulations, and biofilm control.

Conclusion

The synthesis and characterization of pyrazolylthiazole derivatives derived from curcumin analogues demonstrated their structural integrity and biological potential. In vitro antimicrobial evaluations confirmed the effectiveness of these derivatives against bacterial and fungal strains, with some compounds showing enhanced activity. The findings underscore the importance of heterocyclic frameworks, such as pyrazolylthiazoles, in developing potent antimicrobial agents. These results pave the way for further structure-activity relationship studies and the potential optimization of these derivatives for clinical applications, addressing the urgent need for innovative solutions in combating microbial resistance.

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