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Short Communication

Synthesis, biological evaluation and molecular docking study of pyrimidine linked thiazolidinedione derivatives as potential antimicrobial and antitubercular agents

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ABSTRACT

The design and development of novel antimicrobial agents are highly desired to combat the emergence of medication resistance against microorganisms that cause infections. A series of new pyrimidine-linked thiazolidinedione derivatives (**5a-j**) were synthesized, characterized, and their antimicrobial properties assessed in the current investigation. Here, novel pyrimidine-linked thiazolidinedione compounds were designed using the molecular hybridization approach. Elemental and spectral techniques were used to determine the structures of the synthesized hybrids. The majority of compounds showed encouraging antibacterial properties. Among the active compounds, **5g**, **5i**, and **5j** showed 1.85, 1.15, and 1.38 times the activity of streptomycin against *S. aureus*, respectively, with MIC values of 6.4, 10.3, and 8.6 μM. With MIC values of 10.8, 21.9, and 15.4 μM, respectively, the compounds **5g**, **5i**, and **5j** showed 2.14, 1.05, and 1.50 times the activity of linezolid against the methicillin-resistant *S. aureus* (MRSA) strain. Furthermore, when compared to the reference medications, compounds **5g**, **5i**, and **5j** demonstrated broad-range antimicrobial efficacy against all tested strains of bacteria and fungus. Out of all the compounds that were investigated, compounds **5g**, **5i**, and **5j** showed noteworthy anti-tubercular activity. **5g** is the most effective, 1.59 times more effective than reference drug isoniazid. To anticipate the binding manner, the synthesized potent compounds were subjected to molecular docking into the active binding site of MRSA and the mycobacterial membrane protein large 3 (MmpL3) protein. The compounds **5g**, **5i**, and **5j** may eventually serve as lead compounds in the search for antimicrobial and anti-TB therapeutic agents.

A chronic illness, TB is transmitted by airborne droplets of the bacillus Mycobacterium tuberculosis (Mtb). Currently, tuberculosis is the second most common infectious illness worldwide, posing a serious threat to public health.[1] It is among the most common causes of mortality from a single infectious pathogen. The WHO estimates that tuberculosis caused by Mtb claims the lives of 1.5 million people annually.[2] The main health issue is antimicrobial resistance, and TB has the largest number of documented cases of multiple drug resistance among infectious illnesses.[3–4] The primary cause of this disease's extensive distribution is the emergence of medication resistance, which has alarmed researchers worldwide and is currently at an alarming level for several infectious illnesses.[5–6] Numerous methods, including quadruple-drug therapy, have been investigated for the treatment of tuberculosis; nevertheless, these methods fall short of fully eradicating the illness. This presents a challenge to organic synthesis chemists in their quest to develop novel, potent anti-tubercular drugs.[7] Nonetheless, scientists are working hard to find a fresh lead for anti-tubercular medications with cutting-edge modes of action throughout the globe. Similarly, the emergence of drug-resistant bacterial and fungal species necessitates the development of broad-spectrum antimicrobial medicines.

A significant category of organic molecules with several promotional

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