Synthesis, Characterization and Antimicrobial Activity of Isatin-thiosemicarbazone Hybrids

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Abstract:

Globally, the rise of multidrug-resistant (MDR) bacterial infections poses a significant public health threat due to their continuous increase. Traditional single-target drugs often suffer from diminished efficacy due to resistance mechanisms, especially to bacterial pathogens and cancer cells [1]. This situation emphasizes the importance of developing novel molecular scaffolds that employ multiple biological mechanisms. In this context, molecular hybridization is an effective strategy that combines multiple pharmacophoric units into one molecule. This enhances potency and selectivity and overcomes resistance pathways [2]. We report the design, synthesis, and systematic evaluation of a series of quaternary ammonium-Isatin-thiosemicarbazone salt hybrids featuring tunable N-alkyl linkers and styryl or Schiff base -conjugated bridges at the C3 position and water-soluble. This study proposes that molecular hybridization with quaternary ammonium functionality results in compounds that have cooperative dual-target binding and disrupt bacterial membranes at the same time, thereby enhancing antimicrobial potency and reducing toxicity. All synthesized compounds were characterized and confirmed using 1H NMR, 13C NMR, IR, and high-resolution mass spectrometry (HRMS)