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Biological Evaluation and Molecular Modeling Study of Thiosemicarbazide Derivatives as Bacterial Type IIA Topoisomerases Inhibitors

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Abstract : In this contribution, we will describe the inhibitory potency of nine thiosemicarbazide derivatives against bacterial type IIA topoisomerases, their antibacterial profile, and molecular modeling evaluation. We have found that one of the tested compounds, 4-benzoyl-1-(2-methyl-furan-3-ylcarbonyl) thiosemicarbazide, remarkably inhibits the activity of S. aureus DNA gyrase with the IC50 below 5 μM. Besides, this compound displays antibacterial activity on Staphylococcus spp. and E. faecalis at non-cytotoxic concentrations in mammalian cells, with minimal inhibitory concentrations (MICs) values at 25 μg/mL. Based on the enzymatic and molecular modeling studies we propose two factors, i.e. geometry of molecule and hydrophobic/hydrophilic balance as important molecular properties for developing thiosemicarbazide derivatives as potent Staphylococcus aureus DNA gyrase inhibitors.

Keywords : bioactivity, drug design, topoisomerase, molecular modeling
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