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Hypothesis Design, Synthesis, and In Vitro Antituberculosis Activity of 2(5H)-Furanone Derivatives

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Abstract

A series of 2(5H)-furanone-based compounds were synthesized from commercially available mucohalic acids. From the first-generation compounds, three showed inhibitory activity (10 mg/mL) of at least 35% against Mycobacterium smegmatis mc2 155 growth (Bioscreen C system). In screening the active first-generation compounds for growth inhibition against Mycobacterium tuberculosis H37Rv, the most active compound was identified with a minimum inhibitory concentration (MIC99) of 8.07 mg/mL (15.8 mM) using BACTEC 460 system. No cross-resistance was observed with some current first-line anti-TB drugs, since it similarly inhibited the growth of multidrug resistant (MDR) clinical isolates. The compound showed a good selectivity for mycobacteria since it did not inhibit the growth of selected Gram-positive and Gram-negative bacteria. It also showed synergistic activity with rifampicin (RIF) and additive activity with isoniazid (INH) and ethambutol (EMB). Additional time-kill studies showed that the compound is bacteriostatic to mycobacteria, but cytotoxic to the Chinese.