Synthesis of Acetogenin Analogs Comprising Pyrimidine Moieties Linked by Amine Bonds and Their Inhibitory Activity against Human Cancer Cell Lines

Abstract

Here, we synthesized three acetogenin analogs containing pyrimidine moieties linked by amine bonds, which represent the skeleton structure of pyrimidifen, a mitochondrial complex I-inhibiting insecticide. Replacing the pyrimidine moiety linked by the amine bond remarkably enhanced growth-inhibitory activity of the analogs against several human cancer cell lines. Moreover, these analogs selectively and potently inhibited the growth of these human cancer cell lines regardless of the pyrimidine substituents. Furthermore, COMPARE analyses suggested that these analogs inhibited cancer growth by inhibiting mitochondrial complex I. Our study provides insights into the design of acetogenin analogs as novel antitumor agents.