A novel anticancer agent, benzyldihydroxyoctenone, isolated from Streptomyces sp. causes G1 cell cycle arrest and induces apoptosis of HeLa cells

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Abstract

In the course of screening for anticancer agents, a novel active compound, F3-2-5, was isolated from culture broth of Streptomyces sp. KACC91015. Its structure was identified by NMR, MS, and molecular modeling experiments, and confirmed by total synthesis. Growth of HeLa cells was inhibited in a dose-dependent manner by 0.06 to 0.48 mM F3-2-5 over 24 h (IC50: 60 μM). However, F3-2-5 had no antiproliferative effect on normal lymphocytesused as controls. Moreover, it affected both cell cycle regulation and caused apoptosis of the HeLa cells chromatin condensation and DNA fragmentation were observed in cells exposed to 80 M F3-2-5.1)Western blot analysis revealed that F3-2-5 inhibited phosphorylation of pRb and reduced expression of CDK4, CDK6, cyclin D1, and E, while levels of p53 and p21WAF1/CIP1 increased. Taken together, these findings show that F3-2-5 inhibits proliferation of HeLa cells byinducing G1 phase arrest as a consequence ofinhibition of pRb phosphorylation following up-regulation of p21WAF1/CIP1 and p53. Furthermore, apoptosis in HeLa cells treated with F3-2-5 was associated with an increase in Bax and p53, leading to release of cytochrome c, activation of caspase-9, -3, and -8, and cleavage of PARP.

Reference

1. Lowe, S.W., and Lin, A.W., Apoptosis in cancer. (2000) Carcinogenesis 21, 485-495.