albicans are of increasing concern because of the rising incidence of immunosuppression brought about by AIDS, diabetes, cancer therapies, organ transplantation, and other conditions.
In the course of our screening for the specific growth inhibitors against the mycelial phase of C. albicans, we have selected a Streptomyces sp. A6792 from soils. Isolation and purification of compound A6792-2 were performed using silica gel column chromatography, ODS column chromatography, preparative silica gel TLC, and Sephadex LH-20 column chromatography. The molecular weight of compound isolated from Streptomyces sp. A6792 was determined as 844. From several spectral analyses, the compound A6792-2 was identified as IKD-8344. This compound exhibited a potent growth inhibitory activity (MIC : 1.56-25 μg/ml) against the mycelial, but not yeast phase of C. albicans (up to 200 μg/
ml).

[OC-4] [04/20/2001 (Fri) 14:45 - 15:00 / Room 2]

Apicidin, a histone deacetylase inhibitor, induces apoptosis and Fas/Fas ligand expression in human acute promyelocytic leukemia cells

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We previously reported that apicidin, a histone deacetylase inhibitor, arrests human cancer cell growth through selective induction of $p21^{WAF1/Cip1}$. In this study, we evaluated the apoptotic potential of apicidin in human acute promyeolcytic leukemia cells HL60. Treatment of HL60 cells with apicidin caused decrease in viable cell number in a dose dependent manner, concomitant with progressive accumulation of hyperacetylation of histone H4. These effects were paralleled by increase in DNA fragmentation, nuclear morphological change, and apoptotic body formation. In addition, apicidin activated caspase-3 through conversion of the proenzyme form of caspase-3 to the catalytically active effector protease, and caused subsequent cleavages of poly(ADP-ribose)polymerase (PARP) and $p21^{WAF1/Cip}$, substrates of the caspase-3. Incubation with z-DEVD-fmk, a caspase-3 inhibitor, almost completely abrogated activation of caspase-3, DNA fragmentaion, cleavage of PARP and $p21^{WAF1/Cip}$ by apicidin, indicating that apicidin-induced apoptosis might be due to the activation of caspase-3. Moreover, these effects were preceded by increase in translocation of Bax into mitochondria, resulting in release of cytochrome c from mitochondria to cytosol and cleavage of procaspase-9. Addition of cycloheximide greatly inhibited apicidin activation of caspase-3 through interfering with cleavage of procaspase-3, suggesting that apoptotic induction by apicidin is dependent on de novo protein synthesis. Consistent with these results, apicidin increased the expression level of both Fas and Fas ligand transiently, which can initiate the apoptotic signalling pathway. Taken together, the results suggest that apicidin induce apoptosis through selective induction of Fas/Fas ligand, resulting in cytochrome c release from mitochondria to cytosol and subsequent activation of caspase-9 and caspase-3.

Oral Presentations - Field D

[D1. Medicinal Chemistry] [D2. Pharmacognosy] [D3. Oriental Medicine] [D4. Analytical Chemistry]

[OD-1] [04/20/2001 (Fri) 13:30 - 13:45 / Room 3]