Effects of Polyphenolic Anthrone Derivatives, Resistomycin and Hypericin, on Apoptosis in Human Megakaryoblastic Leukemia CMK-7 Cell Line

Yoshihito Shiono[a,*], Nobuyo Shiono[a], Shujiro Seo[b], Syuichi Oka[a] and Yoshimitsu Yamazaki[a]

[a] Research Institute of Biological Resources , National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki 305–8566, Japan. Fax: +81-298-61-6733. E-mail: y.shiono@aist.go.jp

[b] Tokiwa Pharmaceutical Co. Ltd., Sakura, Chiba 285-0801, Japan

* Author for correspondence and reprint requests

Z. Naturforsch. **57 c**, 923–929 (2002); received April 30/June 12, 2002

Resistomycin, Apoptosis, CMK-7

A tetrahydroxyanthrone derivative, resistomycin, was isolated from the culture broth of *Streptomyces sulphureus* and a similar polyphenolic dianthraquinone, hypericin, was isolated from an extract of *Hypericum perforatum* L. as modulators for apoptosis. Resistomycin inhibited apoptosis induced by actinomycin D (AD) with or without acceleration by colcemid (CL) in human megakaryoblastic leukemia CMK-7 cells. IC_{50} for inhibition against AD-induced apoptosis was about 0.5 μM and IC_{50} for inhibition against AD plus CL-induced apoptosis was about 1 μM. CL alone induced weak apoptosis in cells, which was enhanced by resistomycin. Hypericin did not inhibit AD-induced apoptosis and slightly enhanced CL-induced apoptosis. Emodin, corresponding to 1 of 2 anthraquinone units in hypericin, did not show any effect on this apoptotic system. AD-induced apoptosis was inhibited by the antioxidative flavonoid, luteolin (IC_{50} 45 μM), and a protein kinase C (PKC) inhibitor, staurosporine (IC_{50} 1.5 μM), but these compounds did not affect the CL-induced apoptosis. Hypericin and resistomycin scavenged superoxide anion radicals at the same rate as luteolin. PKC in CMK-7 cells was inhibited by hypericin and luteolin, but not significantly inhibited by resistomycin. This result suggests that the inhibition of AD-induced apoptosis by resistomycin is at least partly correlated with its antioxidative activity, and that the enhancement of CL-induced apoptosis by this compound depends upon the lack of PKC inhibitory activity. Though the mechanism is not clear, the enhancement of the CL-induced apoptosis might be hindered by PKC inhibition in the case of hypericin and luteolin.