

# **Induction of Apoptosis by Alkaloids, Non-Protein Amino Acids, and Cardiac Glycosides in Human Promyelotic HL-60 Cells**

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The induction of apoptosis by 66 alkaloids of the quinoline, quinolizidine, pyrrolizidine, isoquinoline, indole, terpene, tropane, steroid, purine, and piperidine type, of 9 cardiac glycosides, 11 non-protein amino acids and 10 further secondary metabolites was assayed in HL-60 cell cultures and measured by quantification of the subdiploid DNA content by flow cytometry, detection of DNA fragmentation by gel electrophoresis, and cell morphology. Several alkaloids of the isoquinoline, quinoline, and indole type were active, whereas quinolizidine, tropane, pyrrolizidine, terpene and piperidine alkaloids were mostly inactive. The proapoptotic alkaloids can be characterized by their property to inhibit protein biosynthesis and their intercalation into DNA at the same time, or by their inhibition of microtubule formation. All cardiac glycosides, which are both membrane detergents and Na<sup>+</sup>,K<sup>+</sup>-ATPase inhibitors, are potent apoptosis inducers. Also proapoptotic were a few non-protein amino acids, podophyllotoxin and the flavonoid quercetin.

*Key words:* Apoptosis, DNA Intercalation, Protein Biosynthesis Inhibition, Microtubule Inhibitor