Emodin induces apoptosis in human promyeloleukemic HL-60 cells accompanied by activation of caspase 3 cascade but independent of reactive oxygen species production.

陳彥州;沈杏娟
Chen YC*;Shen SC;Lee WR;Hsu FL;Lin HY;Ko CH;Tseng SW.

Abstract

Emodin (1,3,8-trihydroxy-6-methylanthraquinone) is an active constituent of Rheum palmatum, and showed inhibitory activity on lipopolysaccharide-induced NO production in our previous study. However, the apoptosis-inducing activity of emodin has remained undefined. Among three structurally related anthraquinones, including emodin, physcion, and chrysophanol, emodin showed the most potent cytotoxic effects on HL-60 cells, accompanied by the dose- and time-dependent appearance of characteristics of apoptosis including an increase in DNA ladder intensity, morphological changes, appearance of apoptotic bodies, and an increase in hypodiploid cells. Emodin at apoptosis-inducing concentrations causes rapid and transient induction of caspase 3/CPP32 activity, but not caspase 1 activity, according to cleavage of caspase 3 substrates poly(ADP-ribose) polymerase and D4-GDI proteins, the appearance of cleaved caspase 3 fragments being detected in emodin- but not physcion- or chrysophanol-treated HL-60 cells. A decrease in the anti-apoptotic protein, Mcl-1, was detected in emodin-treated HL-60 cells, whereas other Bcl-2 family proteins including Bax, Bcl-2, Bcl-XL, and Bad remained unchanged. The caspase 3 inhibitor, Ac-DEVD-CHO, but not the caspase 1 inhibitor, Ac-YVAD-CHO, attenuated emodin-induced DNA ladders, associated with the blockage of PARP and D4-GDI cleavage. Free radical scavenging agents including NAC, catalase, SOD, ALL, DPI, L-NAME and PDTC showed no preventive effect on emodin-induced apoptotic responses, whereas NAC, CAT and PDTC prevented HL-60 cells from ROS (H(2)O(2))-induced apoptosis through inhibition of caspase 3 cascades. Induction of catalase, but not SOD, activity was detected in emodin-treated HL-60 cells by in gel activity assays, and H(2)O(2)-induced intracellular peroxide level was significantly reduced by prior treatment of emodin in HL-60 cells. Our experiments provide evidence that emodin is an effective apoptosis inducer in HL-60 cells through activation of the caspase 3 cascade, but that it is independent of ROS production.