

題名:Differential Apoptotic Effect of Wogonin and Nor-Wogonin Via Stimulation of ROS Production in Human Leukeia Cells.

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摘要:We investigate the roles of methoxyl (OCH(3)) and hydroxyl (OH) substitutions at C8 of flavonoids on their apoptosis-inducing activities. Wogonin (Wog) and nor-wogonin (N-Wog) are structurally related flavonoids, and respectively contain an OH and OCH(3) at C8. In leukemia HL-60 cells, N-Wog exhibited more-potent cytotoxicity than Wog according to the MTT and LDH release assays, and the IC(50) values of Wog and N-Wog in HL-60 cells were 67.5 +/- 2.1 and 21.7 +/- 1.5 microM, respectively. Apoptotic characteristics including DNA ladders, apoptotic bodies, and hypodiploid cells accompanied by the induction of caspase 3 protein processing appeared in Wog- and N-Wog-treated HL-60 cells. Interestingly, an increase in intracellular peroxide production was detected in N-Wog- but not Wog-treated HL-60 cells by the DCHF-DA assay, and the reduction of intracellular peroxide by catalase (CAT) induced by N-Wog significantly reduced the N-Wog- but not the Wog-induced cytotoxic effect according to the MTT assay in accordance with the blocking of DNA ladder formation and caspase 3 and PARP protein processing elicited by N-Wog. We further analyzed the effect of six structurally related compounds, including 5-OH, 7-OH, 5,7-diOH, 5,7-diOCH(3), 7,8-diOCH(3), and 7-OCH(3)-8-OH flavones, on apoptosis induction in HL-60 cells. Results suggested that OH at C5 and C7 is essential for both the apoptosis-inducing activity of flavonoids, and OH at C8 may contribute to apoptosis induction ability. Evidence to support a distinct structure-activity relationship in apoptosis induction of flavonoids is provided for the

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