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Eutigoside from the Leaves of *Eurya emarginata* Induces the Apoptosis of HL-60 Leukemia cells

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The present study was undertaken to examine the cytotoxic effect of extract of *Eurya emarginata* against cancer cells and to develop an anti-cancer agent using components of its leaves. The crude extract of its leaves markedly inhibited the growth of leukemia cells including HL-60. When the HL-60 cells were treated with the extract, DNA fragmentation, morphologic changes and sub-G1 hypodiploid cells were observed. Therefore, the inhibitory effect of *E. emarginata* on the growth of the HL-60 cells appears to arise from the induction of apoptosis. Moreover, the extract markedly reduced c-Myc expression in a time-dependent manner. Eutigoside C showing the cytotoxic effect was isolated from the leaves of *E. emarginata*. Eutigoside C reduced the Bcl-2 protein and mRNA levels in a time-dependent manner, whereas the Bax protein and mRNA expression levels were slightly increased. When HL-60 cells were treated with eutigoside C, the release of cytochrome C from mitochondria into the cytosol was observed. Also, the expressions of the active forms of caspase 9 and 3 were increased and the activation of caspase 3 was demonstrated by the cleavage of Poly(ADP-ribose) polymerase, a vital substrate of effector caspase. The results indicate that the eutigoside C from E. emarginata induce apoptosis of HL-60 cells via the down-regulation of Bcl-2 expression and activation of caspases. [Supported by grant No. R05-2000-000-00146-0 from KOSEF]