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

Soo-Young Park¹, Sang-Chul Kim¹, Jae-Hee Hyoun¹, Nam-Ho Lee², Se-Jae Kim³, Young-Ki Lee¹, Deok-Bae Park¹, Eun-Sook Yoo¹, Hee-Kyoung Kang¹ ∗

¹Department of Medicine, College of Medicine; ²Department of Chemistry, College of Natural Science; ³Department of Life Science, College of Natural Science, Cheju National University, Ara 1-dong, Jeju 690-756, South Korea

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]