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Growth Inhibition of U937 Human Leukemia Cells by Aqueous Extract of *Phellinus linteus* through Induction of Apoptosis

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Phellinus linteus is a traditional herb medicine which has been used for patient suffering from cancer in Oriental medicine. It has been known to have immunomodulatory function, antitumor and immunoenhancing activities. In the present study, it was investigated the biochemical mechanisms of anti-proliferative effects by aqueous extract of *Phellinus linteus* (AEPL) in human leukemia U937 cells. It was found that AEPL could inhibit the cell growth of U937 cells in a dose-dependent manner, which was associated with morphological change and apoptotic cell death such as formation of apoptotic bodies and DNA fragmentation. We observed the up-regulation of pro-apoptotic Bax expression, down-regulation of IAP family expression and proteolytic activation of caspase-3 in AEPL treated U937 cells. However, AEPL did not affect the anti-apoptotic Bcl-2 expression and activity of caspase-9. And it was also observed RT-PCR revealed that AEPL treatment caused a dose-dependent induction of tumor suppressor p53 and cyclin-dependent kinase (Cdk) inhibitor p21*WAF1/CIP1*. Moreover, it was observed a dose-dependent decrease in cyclooxygenase (COX)-2 expression. Additionally, the expression of c-myc, human telomerase reverse transcriptase (hTERT) and telomerase-associated protein (TEP-1) were progressively down-regulated by AEPL treatment. Taken together, these results indicated that the anti-proliferative effects of AEPL were associated with the induction of apoptotic cell death through regulation of several major growth regulatory gene products such as Bcl-2 family

expression and caspase protease activity, and AEPL may have therapeutic potential in human leukemia treatment. [This study was financially supported by grant from Technology Development for Agriculture and Forestry, Ministry of Agriculture and Forestry (No. 202041031SB010).]