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Research Article

Esculetin Induces Apoptosis in Human Leukemia Kasumi-1 cells through Caspase 3 Activation

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Abstract

Objective: AML alone accounts for 20% cases of acute leukemia in children and 80% cases in adults. Among many genetic alterations, the most frequently reported translocation is between chromosomes 8 and 21, t(8; 21) or AML1-ETO. In the past decade, the anti–proliferative effect of various natural compounds including esculetin (a coumarin), has been reported in several leukemic cell lines. We have recently shown that esculetin reduces the half-life of AML1-ETO chimeric mRNA as well as mutated c-Kit transcripts in human monocytic leukemia kasumi-1 cell line harbouring the t(8;21) translocation. In the present study we established the antiproliferating activity of esculetin on kasumi-1 cell line.
Methods: In this study, cytotoxicity of the esculetin on kausmi-1 cells was investigated. The ability of esculetin to induce cell cycle arrest, alter mitochondrial potential, activate Caspase cascade and to express apoptotic markers was investigated through western blotting analysis and flow cytometry methods.
Results and conclusion: The half maximal inhibitory concentration of esculetin in kasumi-1 cells was found to be 100 µM. Ecsuletin arrested the cell cycle at G0/G1 phase in kasumi-1 cells. A significant increase in mitochondrial membrane potential and cytosolic release of cytochrome C was observed in ecsuletin treated kasumi-1 cells. This was accompanied with activation of Caspase 3 and Caspase 8 and enhanced cleavage of phospholipase C (PLC)γ-1. Annexin V apoptotic assay further corrobrated our results that esculetin mediated cytoxicity which is accompanied by cleavage of Caspase 3 is due to apoptosis in kausmi-1 cells.

Key words: Esculetin, AML1-ETO, Kasumi-1, Apoptosis, Caspase 3, Caspase 8.

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