

**DIFFERENTIAL EFFECTS OF APIGENIN ON PROTEIN PHOSPHATASE AND
PROTEIN KINASE IS ESSENTIAL FOR LEUKEMIA CELLS APOPTOSIS
INDUCTION**

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Apigenin, a flavonoid abundantly found in fruits and vegetables, exhibits antiproliferative, anti-inflammatory and antimetastatic activities through poorly defined mechanisms. In the present study, we examined the mechanisms that mediate apigenin-induced-apoptosis. We demonstrated that apigenin induced apoptosis in leukemia cells by the activation of caspase-3. The PTEN activity, a lipid phosphatase that antagonizes PI3K function, was increased in cells treated with apigenin, and the highest effect was observed at 70 μ M. In addition, protein kinase PDK1, responsible for activating serine-threonine kinase Akt, was inhibited in treated cells. In agreement, the phosphorylation of GSK3 β , one of the downstream mediator of Akt pathway, was also impaired. Our results show that apigenin inhibited the PI3K/AKT pathway, responsible for a wide variety of cells functions in response to extracellular signals, included cell proliferation. Together, these results indicated that apigenin provided selective activity to promote caspase-dependent-apoptosis of leukemia cells and uncovered an essential role of PTEN, PDK1 and GSK3 during the induction of apoptosis.