Antiproliferation and induction of caspase-8-dependent mitochondria-mediated apoptosis by β-tocotrienol in human lung and brain cancer cell lines

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ABSTRACT

The pure vitamin isomer, β-tocotrienol has the least abundance among the other vitamin E isomers that are present in numerous plants. Hence, it is very scarcely studied for its bioactivity. In this study, the antiproliferative effects and primary apoptotic mechanisms of β-tocotrienol on human lung adenocarcinoma A549 and glioblastoma U87MG cells were investigated. It was evidenced that β-tocotrienol had inhibited the growth of both A549 (GI50=1.38±0.334μM) and U87MG (GI50=2.53±0.604μM) cells at rather low concentrations. Cancer cells incubated with β-tocotrienol were also found to exhibit hallmarks of apoptotic morphologies including membrane blebbing, chromatin condensation and formation of apoptotic bodies. The apoptotic properties of β-tocotrienol in both A549 and U87MG cells were the results of its capability to induce significant ($P<0.05$) double-strand DNA breaks (DSBs) without involving single-strand DNA breaks (SSBs). β-Tocotrienol is said to induce activation of caspase-8 in both A549 and U87MG cells guided by no activation when caspase-8 inhibitor, z-IETD-fmk was added. Besides, disruption on the mitochondrial membrane permeability of the cells in a concentration- and time-dependent manner had occurred. The induction of apoptosis by β-tocotrienol in A549 and U87MG cells was confirmed to involve both the death-receptor mediated and mitochondria-dependent apoptotic pathways. These findings could potentiate the palm oil derived β-tocotrienol to serve as a new anticancer agent for treating human lung and brain cancers.

Keyword: β-tocotrienol; Antiproliferation; Apoptosis; DNA damage; Caspase-8; Cytochrome c