APIGENIN INDUCES CELL DEATH OF HUMAN CHORIOCARCINOMA THROUGH PI3K AND ERK1/2 MAPK SIGNAL TRANSDUCTION

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As a polyphenolic compounds, apigenin has diverse biological effects against oxidative stress, inflammation, carcinogenesis and metastasis. Although epidemiological and case-control studies indicate chemotherapeutic effects of apigenin in various types of cancers, little is known about the effects of apigenin on choriocarcinoma cells. Therefore, we investigated functional roles of apigenin in JAR and JEG3 cells. Apigenin inhibited proliferative and migratory properties of the JAR and JEG3 cells. However, it induced apoptosis by DNA fragmentation and loss of mitochondrial membrane potentials from choriocarcinoma cells. In addition, apigenin inactivated phosphorylation of protein kinases belonged to PI3K/AKT signaling such as AKT, P70S6K and S6 proteins. Otherwise, it increased phosphorylation of ERK1/2 and P90RSK proteins in the JAR and JEG3 cells. Next, the cell viability of JAR and JEG3 cells was analyzed using pharmacological inhibitors for PI3K (LY294002) and ERK1/2 (U0126) with apigenin. A combination of apigenin with LY294002 or U0126 revealed synergistic anti-proliferative effects on choriocarcinoma cells. Collectively, these results indicate that apigenin may be a novel chemotherapeutic drug inhibiting progression of choriocarcinoma cells via regulating PI3K and ERK1/2 MAPK pathways.

Keywords: apigenin, choriocarcinoma, apoptosis, chemotherapy, signal transduction