Vitamina E. O succinato de tocoferila, radical livre do tocoferol induz apoptose em células do câncer gástrico secundário a estresse oxidativo:
2 trabalhos

Sendo a produção da apoptose secundária ao estresse oxidativo, não é aconselhável o uso clínico no câncer onde a oxidação impera nas mitocôndrias e impede a fosforilação oxidativa. O impedimento mitocondrial facilita a geração de ATP via ciclo de Embden-Meyerof motor da mitose. José de Felippe Junior


Department of Nutrition and Food, Harbin Medical University, Harbin, China.

Abstract

Vitamin E succinate (RRR-alpha-tocopheryl succinate, VES), an efficient inducer of apoptosis, acts as a potent agent for cancer therapy. However, the mechanism by which VES mediates the effects are not yet fully understood. Here we studied the effect of endoplasmic reticulum (ER) stress and unfolded protein response (UPR) on VES-induced apoptosis of SGC-7901 human gastric cancer cells. VES caused cytological changes typical of apoptosis, increased ER dilation and cytosolic Ca(2+) concentration. And endogenous ER stress markers, GRP78 and GRP94 were transcriptionally and translationally altered. In response to VES, induction of CHOP, activation of caspase-4 and JNK were observed. Furthermore, VES also triggered activation of UPR components, including RNA-dependent protein kinase (PKR)-like ER kinase (PERK), activating transcription factor 6 (ATF6), X-box-binding protein 1 (XBP1), and ATF4 in a concentration- and time-dependent manner. Consequently, our results suggest that VES-induced apoptosis is coupled to ER stress and UPR activation in SGC-7901 human gastric cancer cells.

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Department of Nutrition and Food Hygiene, Public Health School, Harbin Medical University, Harbin 150001, Heilongjiang Province, China. wukun@public.hr.hl.cn

Abstract

AIM: To investigate the effects of growth inhibition of human gastric cancer SGC-7901 cell with RRR-alpha-tocopheryl succinate (VES), a derivative of natural Vitamin E, via inducing apoptosis and DNA synthesis arrest.

METHODS: Human gastric cancer SGC-7901 cells were regularly incubated in the presence of VES at 5, 10 and 20 mg x L(-1) (VES was dissolved in absolute ethanol and diluted in RPMI 1640 complete condition media correspondingly to a final concentration of VES and 1 mL x L(-1) ethanol), succinic acid and ethanol equivalents as vehicle (VEH) control and condition media only as untreated (UT) control. Trypan blue dye exclusion analysis and MTT assay were applied to detect the cell proliferation. Cells were pulsed with 37kBq of tritiated thymidine and (3H) TdR uptake was measured to observe DNA synthesis. Apoptotic morphology was observed by electron microscopy and DAPI staining. Flow cytometry and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay were performed to detect VES-triggered apoptosis.

RESULTS: VES inhibited SGC-7901 cell growth in a dose-dependent manner. The growth curve showed suppression by 24.7%, 49.2% and 68.7% following 24h of VES treatment at 5, 10 and 20 mg x L(-1), respectively, similar to the findings from MTT assay. DNA synthesis was evidently reduced by 35%, 45% and 98% after 24h VES treatment at 20 mg x L(-1) and 48 h at 10 and 20 mg x L(-1), respectively. VES induced SGC-7901 cells to undergo apoptosis with typically apoptotic characteristics, including morphological changes of chromatin condensation, chromatin crescent formation/margination, nucleus fragmentation and apoptotic body formation, typical apoptotic sub-G1 peak by flow cytometry and increase of apoptotic cells by TUNEL assay in which 90% of cells underwent apoptosis after 48 h of VES treatment at 20 mg x L(-1).

CONCLUSION: VES can inhibit human gastric cancer SGC-7901 cell growth by inducing apoptosis and DNA synthesis arrest. Inhibition of SGC-7901 cell growth by VES is dose- and time-dependent. Therefore VES can function as a potent chemotherapeutic agent against human gastric carcinogenesis.

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