Vitamina E. Gama tocofrentiol promove a parada do ciclo celular no câncer de mama – 2 trabalhos

06/12/10

gamma-Tocotrienol controls proliferation, modulates expression of cell cycle regulatory proteins and up-regulates quinone reductase NQO2 in MCF-7 breast cancer cells.
Department of Biochemistry and Molecular Biology, New York Medical College, Valhalla, NY 10595, USA.

Abstract

BACKGROUND: Tocotrienols, a subgroup of the vitamin E family, have demonstrated antioxidant and anticancer properties. Differential growth responses among different types of tocotrienols have been observed in breast cancer cells; however, specific bioactivity of each individual tocotrienol remains to be elucidated.

MATERIALS AND METHODS: In this study, the effects of gamma-tocotrienol were examined with regard to its ability to suppress cell proliferation via modulation of cell cycle regulatory protein expression, and also from the perspective of control of cellular oxidoreductive status through regulation of detoxification enzymes, e.g., quinone reductase NQO2, using estrogen receptor-positive MCF-7 human breast cancer cells.

RESULTS: It was shown that treatment by gamma-tocotrienol suppressed MCF-7 cell proliferation in a dose- and time-dependent manner. Growth suppression by gamma-tocotrienol was accompanied by changes in the levels of cell cycle regulatory proteins, notably, Rb/E2F complex, cyclin D1/cdk4 and cyclin B1/cdk1, as exemplified by loss of cyclin D1, inhibition of specific Rb phosphorylation (pRb-p at Thr821), and by the time- and dose-dependent increase in the expression of NQO2.

CONCLUSION: By exerting control on expression of specific cell cycle regulatory proteins in concomitance with suppression of cell proliferation, as well as the induction of NQO2, gamma-tocotrienol offers promise as an added chemopreventive and/or chemotherapeutic agent against breast cancer carcinogenesis.

PMID: 20683025

Anti-proliferative effects of gamma-tocotrienol on mammary tumour cells are associated with suppression of cell cycle progression.
College of Pharmacy, University of Louisiana at Monroe, Monroe, LA, USA.

Abstract

OBJECTIVES: Previous studies have shown that gamma-tocotrienol induces potent anti-proliferative effects on +SA mammary tumour cells in culture; here, investigations have been conducted to determine its effects on intracellular signalling proteins involved in regulating cell cycle progression.

MATERIALS AND METHODS: +SA cells were maintained in mitogen-free defined media containing 0 or 4 micromgamma-tocotrienol, for 48 h to synchronize cell cycle in G(0) phase, and then they were exposed to 100 ng/ml EGF to initiate cell cycle progression. Whole cell lysates were collected at various time points from each treatment group and were prepared for Western blot analysis.

RESULTS AND CONCLUSIONS: Treatment with 4 micromgamma-tocotrienol significantly inhibited +SA cell proliferation over a 4-day culture period. Moreover, this treatment resulted in a relatively large reduction in cyclin D1, cyclin dependent kinase (CDK)4, CDK2 and CDK6 levels, between 4 and 24 h after EGF exposure. Tocotrienol treatment also resulted in a relatively large increase in CDK inhibitor (CKI) p27, prior to and after EGF exposure, but had little effect on levels of CKIs, p21 and p15. Tocotrienol treatment also induced a large relative reduction in retinoblastoma (Rb) protein phosphorylation at ser780 and ser807/811. These findings strongly suggest that anti-proliferative effects of gamma-tocotrienol are associated with reduction in cell cycle progression from G(1) to S, as evidenced by increased p27 levels, and a corresponding decrease in cyclin D1, CDK2, CDK4, CDK6 and phosphorylated Rb levels.
PMID: 19922488