

Abstract

Nutr Cancer. 2010 Aug;62(6):789-94.

Mixed tocotrienols inhibit prostate carcinogenesis in TRAMP mice.

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OBJECTIVE: The biological activities of tocotrienols are receiving increasing attention. Herein, we report the efficacy of a mixed-tocotrienol diet against prostate tumorigenesis in the transgenic adenocarcinoma mouse prostate (TRAMP) mouse model.

METHODS: Male TRAMP mice, 8 wk old, were fed 0.1%, 0.3%, or 1% mixed tocotrienols in AIN-76A diet up to 24 wk old. Likewise, a positive control group consisting of male TRAMP mice and a negative control group consisting of wild-type nontransgenic mice were fed regular AIN-76A diet up to 24 wk old.

RESULTS: Our results show that mixed-tocotrienol-fed groups had a lower incidence of tumor formation along with a significant reduction in the average wet weight of genitourinary apparatus. Furthermore, mixed tocotrienols significantly reduced the levels of high-grade neoplastic lesions as compared to the positive controls. This decrease in levels of high-grade neoplastic lesions was found to be associated with increased expression of proapoptotic proteins BAD (Bcl(2) antagonist of cell death) and cleaved caspase-3 and cell cycle regulatory proteins cyclin dependent kinase inhibitors p21 and p27. In contrast, the expression of cyclins A and E were found to be decreased in mixed-tocotrienol groups.

CONCLUSIONS: Taken together, our results show that by modulating cell cycle regulatory proteins and increasing expression of proapoptotic proteins, mixed tocotrienols suppress prostate tumorigenesis in the TRAMP mice.

PMID: 20661828

