Several mechanisms have been postulated for the anticancer effects of tocotrienols. In this study, for the first time, the anticancer effect of tocotrienols is linked to increased expression of interleukin-24 (IL-24) mRNA, a cytokine reported to have antitumor effects in many cancer models. Tocotrienol isomers (alpha-T3, gamma-T3, and delta-T3) and tocotrienol-rich fraction (TRF) inhibited the growth of the 4T1 murine mammary cancer cells (P<0.05), with IC(50) values 8.99, 4.79, 3.73, and 8.63 μg/mL, respectively. Tumor incidence and tumor load in TRF-supplemented BALB/c mice was decreased by 57.1% and 93.6% (P<0.05), respectively. The induction of the IL-24 mRNA in the 4T1 cells by vitamin E decreased in the following order: delta-T3 > gamma-T3 > TRF > alpha-T3 > alpha-T, which was similar to their antiproliferative effects. The IL-24 mRNA levels in tumor tissues of BALB/c mice supplemented with TRF increased 2-fold when compared with control mice. Increased levels of IL-24 have been associated with inhibition of tumor growth and angiogenesis. Treatment of 4T1 cells with TRF and delta-T3 significantly decreased IL-8 and vascular endothelial growth factor mRNA levels. Hence, we report that tocotrienols have potent anti-angiogenic and antitumor effects that is associated with increased levels of IL-24 mRNA.