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Multifaceted role of gamma-Tocotrienol in cancer therapy

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Gamma-Tocotrienol, a member of Vitamin E super-family has attracted great attention of late for its anti-proliferative and anti-carcinogenic potential against different cancers. For example, our group has recently reported that anti-proliferative and chemo-sensitizing effects of Gamma-tocotrienol are associated with its ability to suppress activation of signal transducers and activator of transcription 3 (STAT3), a pro-inflammatory transcription factor that plays a pivotal role in the survival, proliferation, angiogenesis and chemo-resistance of hepatocellular carcinoma. However, the potential of gamma-tocotrienol to overcome chemo-resistance in gastric cancer, which is one of the deadliest cancers in Asia-pacific region, has never been explored before. Hence, we investigated the efficacy of Gamma-tocotrienol in combination with capecitabine to modulate tumor growth and survival in xenograft mouse model. Gamma-tocotrienol also inhibited expression of various oncogenic proteins, induced PARP cleavage and inhibited NF- κ B activation in gastric cancer cells. *In vivo* studies using xenograft model of human gastric cancer demonstrated that gamma-tocotrienol alone suppressed tumor growth and this effect was further potentiated in conjunction with capecitabine. As compared to the vehicle control, gamma-tocotrienol further suppressed the NF- κ B activation and expression of cyclin D1, COX-2, ICAM-1, MMP-9 and survivin in tumor tissues obtained from treatment groups. Additionally we noted, that gamma tocotrienol can function as a potent inhibitor of angiogenesis in both HUVEC and HCC cells. Overall our results suggest for the first time that gamma-tocotrienol can potentiate the effects of chemotherapy through modulation of multiple biomarkers of proliferation and angiogenesis in diverse cancers.

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