

Constantinou C, Papas A, and Constantinou AI. **Vitamin E and cancer: an insight into the anticancer activities of vitamin E isomers and analogues.** *International Journal of Cancer* 2008 23:739-752.

Current observations in the literature suggest that vitamin E may be a suitable candidate for the adjuvant treatment of cancer. Even though historically most research focused on α -tocopherol, more recent evidence suggests that the other isomers of vitamin E (β -, γ and δ -tocopherols and α -, β -, γ - and δ -tocotrienols) differ in their proapoptotic potencies. The main focus of this communication is the current understanding of the molecular mechanisms regulated by vitamin E isomers and their analogs during the induction of apoptosis. This review highlights that the mitochondria are the major target for the induction of apoptosis by vitamin E isomers and analogs and that the various signaling pathways regulated by these agents are likely to contribute towards maximizing the intrinsic pathway of apoptosis triggered initially by the mitochondria. Overall, the presentation of recent studies from the literature in this communication allows the drawing of the following important conclusions: (i) no direct link exists between the antioxidant activity of each isomer/derivative and proapoptotic potency, (ii) tocotrienols are more effective proapoptotic agents than tocopherols, (iii) synthetic modifications of the naturally occurring compounds may improve their apoptotic potency and (iv) vitamin E isomers and derivatives regulate caspase-independent pathways of apoptosis. The latter combined with the evidence presented in this review regarding the additive or synergistic anticarcinogenic effects obtained when vitamin E analogs are used in combination with other cancer chemotherapeutic agents, supports further research to design the most promising vitamin E derivatives and clinically test them in adjuvant chemotherapeutic treatments. ©2008 Wiley-Liss, Inc.