The value of tocotrienols in the prevention and treatment of cancer. P.W. Sylvester, A. Kaddoumi, S. Nazzal, and K. A. El Sayed, *J. Am. Coll. Nutr.*, 2010, Jun 29 (3 Suppl.), 324S-333S. (Review)

Tocopherols and tocotrienols represent the 2 subgroups that make up the vitamin E family of compounds, but only tocotrienols display potent anticancer activity. Although in vitro experimental evidence has been very promising, oral supplementation of tocotrienols in animal and human studies has produced inconsistent results. However, recent studies have now clarified the reasons for these discrepancies observed between in vitro and in vivo studies. Oral absorption of tocotrienols into the circulation is mediated in large part by carrier transporter systems that display saturation and apparently down-regulation when exposed to high concentrations of tocotrienols. To circumvent these limitations in oral absorption of tocotrienols, investigators have developed novel prodrug derivatives and nanoparticle delivery systems that greatly enhance tocotrienol bioavailability and therapeutic responsiveness. Additional studies have also demonstrated that combined treatment of tocotrienols with other traditional chemotherapeutic agents results in a synergistic anticancer response, and this synergistic response was further enhanced when these agents were encapsulated in a nanoparticle delivery system. Taken together, these findings clarify the limitations of oral tocotrienol administration and provide novel alternative drug-delivery systems that circumvent these limitations and greatly enhance the therapeutic effectiveness of tocotrienols in the prevention and treatment of cancer.