Gamma-Tocotrienol Alleviates Chemotherapy-Induced Cardiotoxicity by Promoting Novel Multiscale Mitochondrial Bioenergetic and Structural Restoration

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Breast cancer remains the most prevalent malignancy among women worldwide. Dose-dense AC-T chemotherapy (Adriamycin, Cyclophosphamide, and Paclitaxel), a commonly prescribed regimen, is associated with significant long-term cardiotoxicity in survivors. Gamma-tocotrienol (GT3) exhibits anti-inflammatory, antifibrotic, and radioprotective properties and has been shown to preserve mitochondrial function. This study investigated the cardioprotective potential of GT3 against chemotherapy-induced cardiac injury using a mouse model. Cryopreserved heart tissues (-80 °C), paraffin-embedded cardiac sections, and electron microscopy grids were used to quantitatively and qualitatively assess cardiac inflammation, structural remodeling, microvascular integrity, and mitochondrial function. AC-T chemotherapy induced significant cardiac inflammation, fibrosis, microvascular rarefaction, and mitochondrial dysfunction. GT3 treatment markedly attenuated these pathological changes by reducing inflammatory responses, limiting adverse cardiac remodeling, preserving microvascular density, and maintaining mitochondrial structure and bioenergetic function. Notably, GT3 prevented chemotherapy-induced mitochondrial fission and swelling. Overall, these findings demonstrate that GT3 confers robust multiscale cardioprotection through mitochondrial preservation and highlight its potential as a promising adjuvant therapy to mitigate chemotherapy-associated cardiotoxicity in breast cancer patients.

Awards Won:
Second Award of $2,400