

## Publication

### Antifibrotic effects of tocotrienols on human Tenon's fibroblasts

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**PURPOSE:** To compare the antifibrotic effect of vitamin E isoforms alpha-, gamma-, and delta-tocotrienol on human Tenon's fibroblasts (hTf) to the antimetabolite mitomycin C. **METHODS:** Antifibrotic effects of alpha- (40, 60, 80, 100, and 120 µM), gamma- (10, 20, 30, and 40 µM) and delta-tocotrienol (10, 20, 30, and 40 µM) on hTf cultures were evaluated by performing proliferation, migration and collagen synthesis assays. Whereas for vitamin E the exposure time was set to 7 days to mimic subconjunctival application, cultures were exposed only 5 min to mitomycin C 100 µg/ml to mimic intraoperative administration. Cell morphology (phase contrast microscopy) as an assessment for cytotoxicity and cell density by measuring DNA content in a fluorometric assay to determine proliferation inhibition was performed on day 0, 4, and 7. Migration ability and collagen synthesis of fibroblasts were measured. **RESULTS:** All tested tocotrienol isoforms were able to significantly inhibit hTf proliferation in a dose-dependent manner (maximal inhibitory effect without relevant morphological changes at day 4 for alpha-tocotrienol 80 µM with 36.7% and at day 7 for alpha-tocotrienol 80 µM with 42.6% compared to control). Degenerative cell changes were observed in cultures with concentrations above 80 µM for alpha- and above 30 µM for gamma- and delta-tocotrienol. The highest collagen synthesis inhibition has been found with 80 µM alpha-tocotrienol (62.4%) and no significant inhibition for mitomycin C (2.5%). Migration ability was significantly reduced in cultures exposed to 80 µM alpha- and 30 µM gamma-tocotrienol (inhibition of 82.2% and 79.5%, respectively, compared to control) and also after mitomycin C treatment (60.0%). Complete growth inhibition without significant degenerative cell changes could only be achieved with mitomycin C. **CONCLUSION:** In vitro, all tested tocotrienol isoforms were able to inhibit proliferation, migration and collagen synthesis of human Tenon's fibroblasts and therefore may have the potential as an anti-scarring agent in filtrating glaucoma surgery.

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