



DOSSIER · SUBSTANCE

Delta-Tocotrienol

Delta-tocotrienol is a member of the **vitamin E family**, specifically one of the **tocotrienols**, which are distinguished from tocopherols by their unsaturated side chains. Research focuses on metabolic, oncological, and inflammatory processes. The most notable finding: most controlled human studies do not investigate its effects in isolation but rather its combination with established therapies or its modulation of biomarkers.

91

STUDIES IN
TOTAL

17

IN HUMANS

6

OF WHICH
CONTROLLED

1

IN ANIMALS

29

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-16

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Delta-Tocotrienol at a glance

ORIGIN:
Delta-tocotrienol is one of four natural tocotrienol forms (alpha, beta, gamma, delta) and belongs to the fat-soluble vitamin E derivatives. It occurs in small quantities in plant oils such as palm oil, rice and barley bran, as well as certain nuts and seeds. Due to its unsaturated side chain, it differs structurally and functionally from tocopherols, which confers greater membrane fluidity and potentially stronger antioxidant and signalling molecule properties.

STUDY EVIDENCE:
91 evaluated publications · 6 controlled human studies · 11 observational studies · 1 review · 1 animal study · 28 cell culture studies

- CURRENT EVIDENCE:**
- **Oncology:** A Phase I study in 25 patients with ductal pancreatic neoplasms showed that delta-tocotrienol (200–3200 mg/day) is safe and achieves bioactive plasma concentrations. It induced apoptosis in neoplastic cells (increased cleaved caspase-3 levels) without dose-limiting toxicities.
 - **Inflammatory conditions (NAFLD)** Two randomised, placebo-controlled studies (n=71) showed that delta-tocotrienol (300 mg twice daily) over 12–24 weeks significantly reduced the Fatty Liver Index, ALT, hs-CRP, and malondialdehyde. Ultrasound examinations confirmed an improvement in hepatic steatosis.
 - **Metabolism: (T2DM)** A randomised study (n=110) with 250 mg delta-tocotrienol daily over 24 weeks showed reductions in fasting blood glucose, HbA1c, HOMA-IR, MDA, hs-CRP, TNF-α, and IL-6. Additionally, inflammation-associated miRNAs were regulated, providing preliminary evidence for metabolic effects.
 - **Metabolism: (prediabetes)** A randomised study (n=77) with 300 mg delta-tocotrienol daily over 12 weeks showed improvements in fasting blood glucose, HbA1c, insulin, and HOMA-IR compared to placebo.
 - **Safety** Multiple controlled studies confirmed the good tolerability of delta-tocotrienol at doses up to 3200 mg/day. Side effects such as mild diarrhoea occurred only sporadically.

- LIMITATIONS:**
- The pharmacokinetics of delta-tocotrienol are complex: low plasma concentrations, rapid metabolism, and variable bioavailability complicate the extrapolation of preclinical dose-response data to humans.
 - The causal contribution of delta-tocotrienol in combination therapies (e.g., with chemotherapeutics) remains unclear, as controlled studies on its standalone effects in such settings are lacking.

ASSESSMENT:
Delta-tocotrienol is a promising form of vitamin E with antioxidant, anti-inflammatory, and potentially antitumour properties. Small, short-term studies with biomarker endpoints provide initial indications for its clinical relevance; larger trials with clinical outcomes are needed to confirm these findings.

1. What Delta-Tocotrienol Is

Delta-tocotrienol is one of four natural **tocotrienol forms** (alpha, beta, gamma, delta) and belongs to the **fat-soluble vitamin E derivatives**. Unlike tocopherols, which are widespread in many foods, tocotrienols are rarer and are often supplemented as extracts. The chemical structure with three double bonds in the side chain confers greater **membrane fluidity** and potentially stronger **antioxidant** and **signalling molecule properties** than tocopherols.

For understanding the study evidence, it is crucial that **delta-tocotrienol** is not equivalent to other forms of vitamin E. **Bioavailability** varies greatly depending on the formulation (e.g., with or without fat), and **plasma levels** often reach only low concentrations after oral administration. Furthermore, it is metabolised more rapidly in the body than tocopherols. Many preclinical studies use **cell cultures** or **animal models**, in which delta-tocotrienol is administered in high doses that are not directly transferable. In humans, **supplements** are typically tested in defined dose ranges, although **pharmacokinetics** and **tissue distribution** are still not fully understood.

2. What the Studies Show in Detail

The key human studies and most important reviews — by application area, with population, duration, preparation, measurement, and results, as reported in the original publications. Numbers are included only where the study specifies them.

Distribution of **controlled human studies** by application area — the numbers are not additive, as one study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Safety and tolerability	4
Metabolism	4
Oncology	3
Inflammatory conditions	3
Oxidative stress	2
Fatigue and stress	2

Oncology

In a preclinical study ⁽¹⁾, the effect of delta-tocotrienol on pancreatic cancer was investigated. In human pancreatic cancer cells and in vivo (animal model), delta-tocotrienol was shown to inhibit NF- κ B activity and reduce cancer cell survival. The combination of delta-tocotrienol with gemcitabine led to a significant enhancement of the antitumour effect, both in vitro and in vivo. The study included the four natural tocotrienol compounds (α -, β -, δ -, γ -tocotrienol), with delta-tocotrienol exhibiting the highest bioactivity. Inhibition of NF- κ B activity was associated with suppression of NF- κ B target genes such as Bcl-X(L), XIAP, and survivin. The study does not specify the dose used in the animal model but demonstrated efficacy in human cell lines and in vivo. A limitation is that these are preclinical data not yet validated in humans.

A Phase I study ⁽⁷⁾ examined the safety, pharmacokinetics, and pharmacodynamic effects of delta-tocotrienol in 25 patients with ductal pancreatic neoplasms. Participants received oral doses of 200 to 3200 mg daily for 13 days prior to surgery and a single dose on the day of surgery. No dose-limiting toxicities occurred, and only one patient reported mild diarrhoea at the highest dose (3200 mg/day). The half-life of delta-tocotrienol was approximately 4 hours, with plasma concentrations variable but reaching bioactive levels. A significant induction of apoptosis in neoplastic cells (measured by increased cleaved caspase-3 levels) was observed at doses of 400 to 1600 mg/day. The study shows that delta-tocotrienol is safe and biologically active, though data on long-term efficacy or clinical endpoints such as survival time are lacking.

A Phase II study ⁽⁵⁾ involving 80 women with newly diagnosed breast cancer investigated the effect of delta-tocotrienol in combination with standard neoadjuvant therapy. Participants were randomised to receive either standard therapy alone or in combination with 300 mg delta-tocotrienol twice daily. No difference in response rate or incidence of serious adverse events was observed between the two groups. The study developed a multiplex ddPCR assay for detecting circulating tumour DNA (ctDNA), which demonstrated increased sensitivity through a combination of breast tissue-specific and cancer-associated methylation markers. However, no association was found between ctDNA status and pathological response. The study is limited by its small sample size and lack of dose-response analysis.

In a preclinical study ⁽⁸⁾ on non-small cell lung cancer (NSCLC) cells, delta-tocotrienol was shown to inhibit cell growth, migration, and invasiveness in a dose- and time-dependent manner, as well as induce apoptosis. The antitumour effect was associated with downregulation of Notch-1, Hes-1, survivin, MMP-9, VEGF, and Bcl-XL, and inhibition of NF- κ B DNA-binding activity. The study suggests that delta-tocotrienol, through inhibition of the Notch-1 pathway and NF- κ B, may represent a promising strategy for preventing tumour progression in NSCLC. A limitation is that the results were obtained exclusively in vitro, with no clinical data available.

Another preclinical study ⁽¹⁰⁾ investigated the effect of delta-tocotrienol on pancreatic cancer stem cells and metastasis. Delta-tocotrienol inhibited the viability, survival, and self-renewal of cancer stem cells in three models, as well as the expression of the transcription factors Oct4 and Sox2. Furthermore, migration, invasion, and biomarkers of epithelial-mesenchymal transition (EMT), as well as angiogenesis in pancreatic carcinoma cells and tumours, were suppressed. In an orthotopic metastasis model (L3.6pl), delta-tocotrienol significantly reduced tumour growth and metastasis formation. In a xenograft model using human gemcitabine-resistant pancreatic cancer stem cells, growth and metastasis were also significantly inhibited. The study presents promising preclinical data; however, clinical studies are lacking to validate these findings.

HYPOTHESIS The preclinical and early clinical data suggest that delta-tocotrienol may exert antitumour effects via multiple signalling pathways (NF- κ B, Notch-1, EMT). Combination with standard chemotherapeutic agents such as gemcitabine appears to enhance efficacy without increasing toxicity. However, clinical trials with hard endpoints (e.g., overall survival) are still pending, and the translatability of preclinical models to humans remains uncertain. What is lacking are large-scale, randomised clinical trials with clearly defined oncological endpoints and longer-term follow-up periods.

Inflammatory Processes

In a randomised, double-blind, placebo-controlled pilot study ⁽²⁾, the effect of delta-tocotrienol was investigated in 71 patients with non-alcoholic fatty liver disease (NAFLD). Participants received either 300 mg of delta-tocotrienol twice daily or placebo for 12 weeks. Following the intervention, the delta-tocotrienol group showed a significant reduction in the Fatty Liver Index (FLI), alanine aminotransferase (ALT), high-sensitivity C-reactive protein (hs-CRP), and malondialdehyde (MDA) compared to the placebo group. However, the study has limitations, including the short intervention duration and the absence of histological confirmation of liver changes. Additionally, no dose-response relationship was examined.

A further randomised, placebo-controlled study ⁽³⁾ involving 71 NAFLD patients investigated the effect of 300 mg of delta-tocotrienol twice daily over 24 weeks. Compared to placebo, delta-tocotrienol led to a significant reduction in FLI (-8.52 points), HOMA-IR (-0.37), hs-CRP (-0.61 mg/L), MDA (-0.91 nmol/mL), ALT (-8.86 U/L), and AST (-6.6 U/L). Ultrasound examination showed an improvement in hepatic steatosis. The study showed anti-inflammatory and antioxidant effects of delta-tocotrienol but is limited by the absence of liver biopsy and the small sample size.

In a randomised, controlled study ⁽⁴⁾ involving 110 patients with type 2 diabetes mellitus (T2DM), the effect of 250 mg of delta-tocotrienol daily over 24 weeks on glycaemic control, oxidative stress, and inflammatory markers was investigated. Compared to placebo, delta-tocotrienol led to a significant reduction in fasting blood glucose (-0.48 mmol/L), HbA1c (-0.53%), HOMA-IR (-0.67), MDA (-0.34 nmol/mL), hs-CRP (-0.35 mg/L), tumour necrosis factor- α (TNF- α ; -1.22 pg/mL), and interleukin-6 (-2.30 pg/mL). Furthermore, a more than twofold downregulation of miRNA-375, miRNA-34a, and miRNA-21, as well as an upregulation of miRNA-126 and miRNA-132, was observed. The study demonstrates that delta-tocotrienol exerts anti-inflammatory and antioxidant effects in T2DM; however, data on long-term safety and efficacy are lacking.

HYPOTHESIS The studies suggest that delta-tocotrienol may have positive effects on metabolic-inflammatory diseases such as NAFLD and T2DM through its antioxidant and anti-inflammatory properties. The reduction in inflammatory markers such as hs-CRP and TNF- α , as well as the improvement in insulin resistance, indicate that delta-tocotrienol could be a promising approach to support the treatment of these conditions. However, long-term studies with clinically relevant endpoints (e.g., liver fibrosis, cardiovascular events) and studies on optimal dosing and combination with other therapies are lacking.

Metabolism

In a randomised, controlled study ⁽⁶⁾ involving 77 participants with prediabetes, the effect of 300 mg of delta-tocotrienol daily over 12 weeks on glycaemic parameters was investigated. The delta-tocotrienol group showed a significant reduction in fasting blood glucose (-0.48 mmol/L), HbA1c (-0.53%), insulin (-1.19 μ U/mL), and HOMA-IR (-0.67) compared to the placebo group. The study suggests that delta-tocotrienol may improve glycaemic control in prediabetes.

but is limited by its short duration and the absence of long-term data. Additionally, no dose-response relationship was examined.

An earlier observational study ⁽⁹⁾ in humans and hamsters investigated differences in the plasma transport kinetics and tissue concentrations of tocopherols and tocotrienols. In hamsters, it was found that tocotrienols rapidly disappear from plasma after oral administration and are deposited in adipose tissue in association with triglycerides—a preclinical finding. In humans, supplementation with tocotrienols did not lead to a significant increase in fasting plasma concentrations; however, the concentration of delta-tocotrienol in platelets doubled. The study demonstrates that tocotrienols exhibit different pharmacokinetics compared to tocopherols, which is relevant for interpreting efficacy studies. A limitation is that no clinical endpoints were investigated, and the tissue distribution in humans remains unconfirmed, as the findings are based on preclinical models.

HYPOTHESIS The available data suggest that delta-tocotrienol may have positive effects on glucose metabolism, particularly in prediabetes and T2DM. The differing pharmacokinetics compared to tocopherols may explain why delta-tocotrienol is biologically active despite low plasma concentrations. However, studies on long-term efficacy, optimal dosing, and potential interactions with other antidiabetic agents are lacking.

Overall Picture

Delta-tocotrienol shows promising effects in preclinical models across oncology, inflammatory processes, and metabolism. In oncology, preclinical data suggest that delta-tocotrienol may exert antitumour effects through the inhibition of signalling pathways such as NF-κB and Notch-1 and may enhance the efficacy of chemotherapeutic agents like gemcitabine. However, these findings have not been investigated in humans, and clinical studies with hard endpoints are lacking. In the areas of inflammation and metabolism, randomised controlled trials showed that delta-tocotrienol has antioxidant, anti-inflammatory, and metabolically favourable effects in NAFLD, T2DM, and prediabetes. The reduction in inflammatory markers and improvement in insulin resistance are consistent, but long-term studies with clinically relevant endpoints are lacking.

The evidence base for delta-tocotrienol is still in its early stages in many areas. While preclinical data suggest a broad spectrum of activity, clinical studies are often small, of short duration, and lack histological or hard clinical endpoints. The pharmacokinetics of delta-tocotrienol are complex and differ significantly from those of tocopherols, complicating the interpretation of the data. Systematic studies on optimal dosing, long-term safety, and combination with standard therapies are lacking in all investigated areas.

Methodology of the evidence base

["The studies on delta-tocotrienol encompass a broad range of designs, from preclinical in vitro and animal models to randomised controlled clinical trials. Preclinical studies ^(1, 8, 10) typically investigate effects on cell lines or animal models, focusing on endpoints such as cell viability, apoptosis, pathway activation, and tumour growth. These findings are considered preliminary and require confirmation in human trials, as they do not yet demonstrate effects in humans. Among the human studies, Phase I or Phase II trials with small sample sizes (n=25–110) and short intervention periods (12–24 weeks) predominate. Typical endpoints include safety, pharmacokinetics, biochemical markers (e.g., inflammatory parameters, liver enzymes), and surrogate parameters (e.g., FFI, HOMA-IR). Systematically lacking are large-scale, randomised studies with hard clinical endpoints (e.g., survival, cardiovascular events, liver fibrosis) and long-term studies on safety and efficacy. Additionally, the pharmacokinetics of delta-tocotrienol are not yet fully understood, which complicates the interpretation of dose-response relationships."]

Delta-tocotrienol: Adjuvant or standalone agent?

The

CONTROLLED HUMAN STUDIES

almost exclusively examine delta-tocotrienol as a **support to established therapies** or for **modulating biomarkers**. For example, in **oncological research**, the **combination with gemcitabine** is investigated, with delta-tocotrienol intended to suppress **NF-κB activation**. However, whether these effects are **clinically relevant** or merely **laboratory phenomena** remains unclear. The **most cited study** (2011) demonstrates an **enhancement of gemcitabine's antitumour activity**, yet the **contribution of delta-tocotrienol** to the overall effect cannot be quantified. A similar situation exists in **metabolic studies**: here, **liver enzymes** or **oxidative stress** are measured, but not **hard endpoints** such as liver fibrosis or diabetes complications.

A further issue is the

LACK OF STANDARDISATION

in **formulations**. Delta-tocotrienol is used in studies as a **pure substance**, in **oil form**, or as an **enriched supplement**, which complicates **comparability**. Moreover, it is unclear whether the **measured plasma levels** correlate with **tissue concentration**—a critical factor for **efficacy in target organs** such as the liver or tumour tissue. **Research in this area is still in its infancy**: while preclinical data provide **mechanistic hypotheses**, **large, randomised studies** examining delta-tocotrienol as a **monotherapy** or in **clinically relevant combinations** are lacking. However, the **pioneering work** of early studies (e.g., on **miRNA regulation** in lung cancer cells) demonstrates that the field is **promising from a basic science perspective**.

3. How Robust the Research Is

Of the **91 evaluated studies**, **17 are human studies**, of which **6 are controlled trials**. The research is distributed across **basic investigations** (43), **cell culture studies** (28), and **observational human studies** (11). The controlled studies focus on **safety**, **metabolic parameters** (e.g., in non-alcoholic fatty liver disease), **oncology** (combination therapies), and **inflammatory markers**. The most cited human studies primarily examine delta-tocotrienol as an **adjuvant therapy** or for **modulating biomarkers**, rather than as a standalone intervention. Preclinical data dominate, with mechanisms such as **NF-κB inhibition**, **miRNA regulation**, or **mitochondrial dysfunction**.

The **robustness of human studies** is limited: the **sample sizes** are small, and the **observation periods** are short. The **most cited controlled studies** (e.g., on pancreatic cancer or fatty liver) show **changes in laboratory parameters**, not clinical endpoints such as survival or disease progression. The **combination with chemotherapeutic agents** (e.g., gemcitabine) is frequently investigated, but the **causal contribution** of delta-tocotrienol remains unclear. Methodologically weak are **observational studies** that describe **associations** (e.g., between tocotrienol levels and disease risk) without testing **causality**. The **translatability** of cell culture and animal data to humans is limited, as **supraphysiological doses** are often used in these models.

4. What Is Often Claimed — and What the Data Show

STATEMENT	EVIDENCE BASE
Delta-tocotrienol reduces inflammatory markers in fatty liver	Controlled studies demonstrate changes in liver enzymes and oxidative stress , but not an improvement in liver histology or clinical endpoints such as fibrosi
Delta-tocotrienol enhances the efficacy of chemotherapy	The combination with gemcitabine demonstrates enhanced antitumour activity in one study, yet the causal contribution of delta-tocotrienol remains unclear.
Delta-tocotrienol helps prevent diabetes	A study on prediabetes shows improvements in blood glucose levels , but the sample size is small and the observation period is short . There are no long-ter
Delta-tocotrienol exhibits stronger antioxidant effects than tocopherols	Preclinical data suggest a higher antioxidant capacity , but direct comparisons in humans are lacking . The clinical relevance of these laboratory findings rem

5. Profile: Molecule and Charge

Delta-tocotrienol is not a single molecule but a **mixture**—there is no molecular formula or fixed molecular mass. What can be described are functional groups, charge behaviour, and redox properties; this is precisely what the next section addresses.

6. Charge, Electrons, Radicals

Delta-Tocotrienol demonstrates electrochemical properties indicative of redox processes. In cell cultures, an oxidative conversion of delta-tocotrienol to a quinone derivative (δ-T3Q) was observed, suggesting electron transfer reactions ¹⁷. This transformation implies that the substance is capable of generating reactive oxygen species (ROS) ¹⁸. Additionally, foundational studies have described a reduction in ROS production by delta-tocotrienol, indicating a regulatory role in redox balance ¹⁹. Whether these effects are directly attributable to charge or cation exchange processes remains unclear in the available studies. No measurements in humans exist for these specific electrochemical properties.

In vitro, the antioxidant activity of delta-tocotrienol and related compounds was examined using the DPPH radical-scavenging assay, indicating an interaction with free radicals. The observed effects in cell cultures (e.g., SKBR3 mitochondria) suggest involvement in redox reactions, although the precise nature of electron transfer or charge displacement is not detailed ^{17 18}. Animal or human studies on electrochemical parameters such as cation exchange or specific redox potentials are lacking. Whether the ROS generation or modulation demonstrated in cell cultures ^{18 19} is due to direct electrochemical mechanisms requires further investigation. Tissue or human studies to clarify this question are pending.

7. Interactions with Other Substances

Substances from this platform that have been **jointly** investigated or discussed with this compound in human studies and reviews—whether in combination, comparison, or shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic inflammation	5	3

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Resveratrol	3	2
Stress, cortisol and inflammation	3	2
Therapeutic fasting and intermittent fasting	2	1

In cell cultures, delta-tocotrienol enhanced the effects of chemotherapeutic agents such as jerantinine B, enabling a dose reduction of up to 3.8-fold. Synergistic effects were also observed with vemurafenib in resistant melanoma cells, where delta-tocotrienol restored responsiveness²¹. Additive cytotoxic effects occurred in combination with Src and Stat3 inhibitors. Delta-tocotrienol induced cell cycle blockade in the G1-S phase and mitochondrial apoptosis, suggesting potential pharmacodynamic interactions^{20 21}.

In humans, the bioavailability of delta-tocotrienol following oral administration has been confirmed, with significant increases in plasma levels¹¹. A controlled study examined its combination with neoadjuvant standard therapy in breast cancer patients, without reporting specific interactions with enzymes such as CYP^{5 5}. Uptake or binding to other nutrients was not analysed. Potential interactions with pharmaceuticals or nutrients via enzyme systems (e.g., CYP) cannot be inferred from the available data. Further studies on pharmacokinetics and possible interactions would be necessary.

8. Overdose, Tolerability, and Limits

Data on overdose, toxicity, and upper limits of delta-tocotrienol are limited. In a Phase I study involving patients with ductal pancreatic neoplasms, doses ranging from 200 to 3200 mg daily were administered over 13 days without reaching dose-limiting toxicity or a maximum tolerated dose^{7 7}. One patient reported diarrhoea at a daily dose of 3200 mg⁷. In healthy volunteers, single doses of 100 to 1600 mg and multiple doses over 14 days were tested without adverse events^{11 11}.

There are no specific contraindications indicated in the available studies. Adverse effects were rarely documented in controlled human studies. In a preoperative study of delta-tocotrienol in pancreatic neoplasms, diarrhoea occurred once at a daily dose of 3200 mg⁷. Whether interactions with other substances exist is not evident from the evidence. Further investigations into long-term use and higher dosages would be required.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full evaluation includes significantly more studies; here, only the most reliable are listed.

Controlled Human Studies

- ¹ Vitamin E δ -tocotrienol augments the antitumor activity of gemcitabine and suppresses constitutive NF- κ B activation in pancreatic cancer (2011)
- ² Effects of Delta-tocotrienol Supplementation on Liver Enzymes, Inflammation, Oxidative Stress and Hepatic Steatosis in Patients with Nonalcoholic Fatty Liver Disease (2018)
- ³ Delta-tocotrienol supplementation improves biochemical markers of hepatocellular injury and steatosis in patients with non-alcoholic fatty liver disease (2020)
- ⁴ Effects of delta-tocotrienol supplementation on glycaemic control, oxidative stress, inflammatory biomarkers and miRNA expression in type 2 diabetes mellitus (2021)
- ⁵ Phase II trial of delta-tocotrienol in neoadjuvant breast cancer with evaluation of treatment response using circulating tumour DNA (2023)
- ⁶ Effects of delta-tocotrienol supplementation on glycaemic control in individuals with prediabetes: a randomised controlled study (2022)

Observational Human Studies

- Natural forms of vitamin E as effective agents for cancer prevention and therapy (2017)
- ⁷ A Phase I safety, pharmacokinetic, and pharmacodynamic presurgical trial of vitamin E δ -tocotrienol in patients with pancreatic ductal neoplasia (2015)
- ⁸ Inhibition of cell growth and induction of apoptosis in non-small cell lung cancer cells by delta-tocotrienol is associated with Notch-1 downregulation (2011)
- ⁹ Differences in the plasma transport and tissue concentrations of tocopherols and tocotrienols: observations in humans and hamsters (1993)
- ¹⁰ δ -Tocotrienol, a natural form of vitamin E, inhibits pancreatic cancer stem-like cells and prevents pancreatic cancer metastasis (2017)
- ¹¹ Pharmacokinetics and safety of vitamin E δ -tocotrienol after single and multiple doses in healthy subjects with measurement of vitamin E metabolites (2016)
- ¹² Delta-tocotrienol inhibits non-small-cell lung cancer cell invasion via the inhibition of NF- κ B, uPA activator, and MMP-9 (2018)
- ¹³ A 12-week evaluation of annatto tocotrienol supplementation for postmenopausal women: safety, quality of life, body composition, physical activity, and bone health (2018)
- ¹⁴ δ -Tocotrienol feeding modulates gene expression of EIF2, mTOR, and protein ubiquitination through multiple signalling pathways in patients with chronic hepatitis C (2018)
- ¹⁵ Delta-tocotrienol induces apoptotic cell death via depletion of intracellular squalene in ED40515 cells (2014)

Studies on Human Tissue

- ¹⁶ Anticancer activity of delta-tocotrienol in human hepatocellular carcinoma: involvement of autophagy induction (2024)

10. Summary

Delta-tocotrienol shows consistent effects on metabolic and inflammatory laboratory parameters in controlled human studies. In non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM), significant reductions in inflammatory markers (hs-CRP, TNF- α), oxidative stress (MDA), and insulin resistance (HOMA-IR) have been documented. These findings are based on surrogate endpoints and do not yet demonstrate clinical outcomes. Oncological Phase I studies confirm safety in pancreatic cancer, while the induction of apoptosis has so far been shown only in preclinical cell studies, without clinical endpoints. Pharmacokinetic data suggest rapid tissue distribution despite low plasma levels, complicating the interpretation of preclinical high-dose models.

HYPOTHESIS Preclinical and early clinical data suggest that delta-tocotrienol may exert effects in oncology, anti-inflammation, and metabolic modulation through mechanisms such as NF- κ B inhibition, miRNA regulation, and antioxidant activity. Combination with standard therapies (e.g., gemcitabine in pancreatic cancer) appears to enhance efficacy without increasing toxicity. In metabolic diseases, delta-tocotrienol could serve as an adjuvant therapy to improve glycaemic control and reduce inflammatory markers. However, its impact on hard clinical outcomes (e.g., liver fibrosis, cardiovascular events, overall survival) and optimal dosing, as well as interactions with established therapies, have not yet been systematically investigated.

Future studies should address the following open questions: 1) Long-term safety and efficacy in large, randomised cohorts with hard clinical endpoints (e.g., survival in oncology, progression from NAFLD to fibrosis). 2) Systematic dose-finding studies to optimise bioavailability and tissue distribution, particularly in comparison with other vitamin E forms. 3) Mechanistic studies to clarify the causal contribution of delta-tocotrienol in combination therapies, for example, through placebo-controlled designs with monotherapy. 4) Pharmacokinetic investigations into tissue accumulation and metabolism in humans to improve the translatability of preclinical models.

11. Open Questions

- **Clinical endpoints:** Whether delta-tocotrienol influences **hard clinical outcomes** (e.g., survival, disease progression) remains untested. **Large, randomised studies** with **long durations** are required.
- **Tissue specificity:** It remains unclear whether **plasma levels** correlate with **concentrations in target tissues** (e.g., liver, tumour). **Pharmacokinetic studies** with **tissue analyses** are lacking.
- **Monotherapy:** Nearly all controlled studies examine delta-tocotrienol as an **adjuvant**. Whether it is **effective alone** remains an open question.

12. Further Paths

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

- Interaction network

Frequently Asked Questions

Why is delta-tocotrienol often combined with chemotherapy?

The **most frequently cited controlled study** (2011) demonstrates that delta-tocotrienol enhances the **antitumour activity of gemcitabine** and suppresses **NF- κ B**, a signalling pathway associated with **therapy resistance**. The combination aims to overcome **resistance mechanisms**. However, whether this is **clinically relevant** remains unclear, as **survival data** are lacking. Research is investigating delta-tocotrienol here as an **adjuvant therapy**, not as a standalone agent.

How does delta-tocotrienol differ from other forms of vitamin E?

Delta-tocotrienol belongs to the **tocotrienols**, which differ from **tocopherols** by their **unsaturated side chains**. This results in **greater membrane fluidity** and potentially **stronger antioxidant** and **signalling molecule effects**. Preclinical data suggest **distinct mechanisms of action**, such as **inhibition of HMG-CoA reductase** or **miRNA regulation**. However, in humans, its **bioavailability** and **tissue distribution** are **less well studied** than those of tocopherols.

Can delta-tocotrienol be used in non-alcoholic fatty liver disease?

Two controlled studies show **improvements in liver enzymes, oxidative stress, and hepatic steatosis in NAFLD patients**. However, these effects are **biomarker-based** and have not been validated with **histological or clinical endpoints**. The **sample sizes** are small, and the **long-term effects** are unknown. Delta-tocotrienol is being investigated here as a **supportive therapy**, not as a **causal treatment**.

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- 4 Effects of delta-tocotrienol supplementation on Glycemic Control, oxidative stress, inflammatory biomarkers and miRNA expression in type 2 diabetes mellitus: A randomized control trial
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- 6 Effects of delta-tocotrienol supplementation on glycaemic control in individuals with prediabetes: A randomized controlled study
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- 7 A Phase I Safety, Pharmacokinetic, and Pharmacodynamic Presurgical Trial of Vitamin E δ -tocotrienol in Patients with Pancreatic Ductal Neoplasia
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Husain K, Centeno BA, Coppola D, Trevino J, Sebt SM, Malafa MP · 2017
- 11 Pharmacokinetics and safety of vitamin E δ -tocotrienol after single and multiple doses in healthy subjects with measurement of vitamin E metabolites
Mahipal A, Klapman J, Vignesh S, Yang CS, Neuger A, Chen DT et al. · 2016
- 12 Delta-tocotrienol inhibits non-small-cell lung cancer cell invasion via the inhibition of NF- κ B, uPA activator, and MMP-9
Rajasinghe LD, Pindiprolu RH, Gupta SV · 2018
- 13 A 12-week evaluation of annatto tocotrienol supplementation for postmenopausal women: safety, quality of life, body composition, physical activity, and nutrient intake
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