

Article

High-Stability Lycopene Lipid Delivery and Endothelial Function: A Cardiometabolic Evidence Framework

Yassine Igoundaz¹, Aaron Scott², Xavier Quinn³
^{1,2,3}. National Laboratory of Medicine LLC

Citation: Igoundaz Y. High-Stability Lycopene Lipid Delivery and Endothelial Function: A Cardiometabolic Evidence Framework. American Journal of Biology and Natural Sciences 2026, 3(9), 139-144.

Received: 10th May 2026

Revised: 11th Jul 2026

Accepted: 20th Aug 2026

Published: 24th Sept 2026


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Abstract: A high-stability lycopene lipid matrix was evaluated as a controlled exposure platform for cardiovascular nutrition research. Across three optimized formulations, total lycopene was 2.13-2.34%, all-trans lycopene 85.1-86.2%, peroxide value 1.8-2.0 mmol/kg, and 30-day lycopene retention at 45°C was 90.8-91.6%. Human evidence was considered by endpoint rather than collapsed into a single cardiovascular effect. In statin-treated patients with cardiovascular disease, 7 mg/day lycopene for two months improved endothelium-dependent vasodilatation by 53%, while the healthy-volunteer arm showed no comparable change. Meta-analyses report variable findings across blood pressure, lipids, inflammation, and endothelial measures. More recent randomized tomato-juice work also shows that flow-mediated dilation can improve even when measured oxidative-stress markers do not move in parallel. The formulation data provide a stable lipid-phase lycopene input for studies that prospectively define vascular phenotype, circulating lycopene exposure, and the primary cardiometabolic endpoint.

Keywords: lycopene; endothelial function; cardiovascular health; blood pressure; carotenoids; lipid matrix; oxidative stress; NVTIA®

Introduction

Lycopene has been studied across several cardiovascular domains, including endothelial function, blood pressure, lipid oxidation, and serum lipids. Those outcomes respond on different time scales and are influenced by baseline vascular status, background medication, dose, and food matrix. An endothelial response therefore should not be treated as interchangeable with a lipid or blood-pressure response.

Formulation can add another layer of variability. Lycopene is fat soluble, and processing, oil association, isomer distribution, and storage oxidation influence the composition presented to the gastrointestinal tract. The lipid matrix evaluated here uses low-oxygen enrichment with MCT, high-oleic sunflower oil, mixed tocopherols, and L-ascorbyl palmitate to reduce that source of exposure drift.

We examined formulation stability first and then read the clinical literature by endpoint and population. The aim was to identify where a stable lycopene exposure is most useful for direct study, not to combine heterogeneous cardiovascular trials into one efficacy estimate.

Materials and Methods

Formulation and analytical evaluation

Lycopene-rich tomato peel was processed by acidic low-temperature enzymatic disruption and ethanol replacement dehydration. A deoxygenated oil phase containing caprylic/capric triglyceride, high-oleic sunflower oil, mixed tocopherols, and L-ascorbyl palmitate was used for 2-4 cyclic enrichment stages under nitrogen and light protection. Total lycopene, all-trans proportion, moisture, residual ethanol, peroxide value, and accelerated-storage performance were measured.

Evidence framework

Human evidence through August 2026 was selected from randomized trials, systematic reviews, meta-analyses, and umbrella reviews covering endothelial function, blood pressure, serum lipids, inflammation, and oxidative stress. Study population, baseline cardiovascular status, dose, duration, and delivery format were retained because they repeatedly modified the observed response.

Results

Stable composition relevant to lipid delivery

Table 1. Analytical quality of the optimized NVTIA® lycopene lipid formulations

Formulation	Transfer rate (%)	Total lycopene (%)	All-trans (%)	Moisture (%)	Ethanol residue (%)	PV (mmol/kg)
F1	80.8	2.28	85.6	0.22	0.06	1.9
F2	78.2	2.13	86.2	0.25	0.07	2.0
F3	82.1	2.34	85.1	0.20	0.05	1.8

Table 2. Accelerated stability of the optimized lycopene lipid formulations

Formulation	30-d lycopene retention (%)	Δ all-trans proportion (percentage points)	Sediment (%)	Appearance
F1	91.6	-3.1	0.9	Uniform dark-red oily liquid
F2	90.8	-2.9	1.0	Uniform dark-red oily liquid
F3	91.2	-3.3	0.8	Uniform dark-red oily liquid

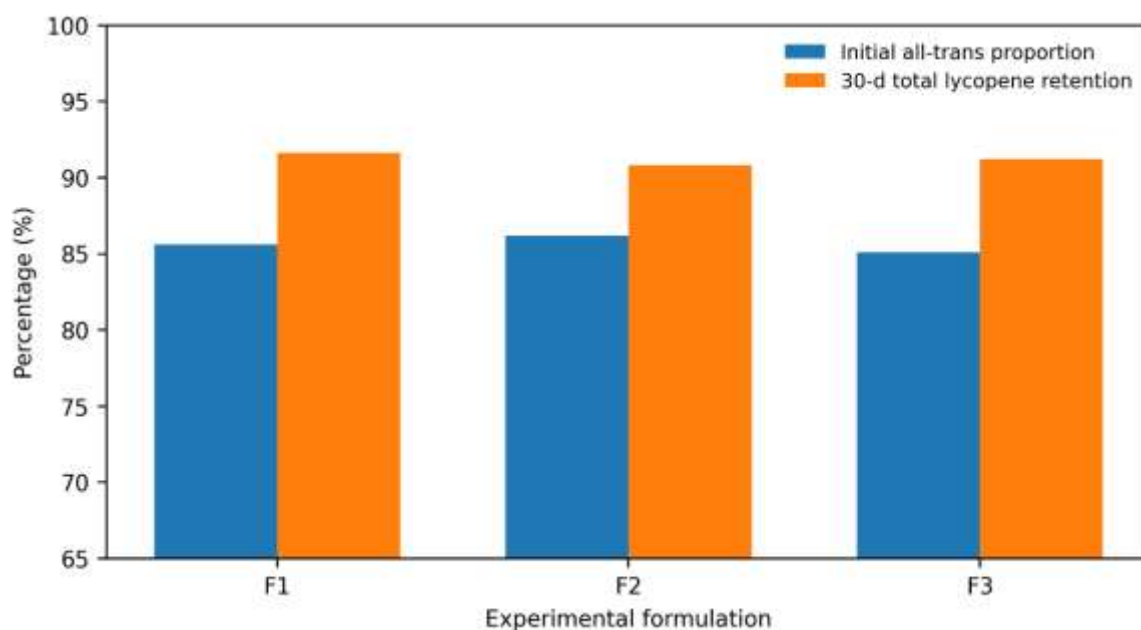


Figure 1. Initial all-trans lycopene proportion and 30-day total lycopene retention in the three optimized formulations. Both endpoints are expressed as percentages and plotted from direct analytical values.

The optimized formulations clustered tightly: total lycopene 2.13-2.34%, all-trans lycopene 85.1-86.2%, peroxide value 1.8-2.0 mmol/kg, and 30-day lycopene retention 90.8-91.6%. Sediment remained at or below 1.0%. These values describe the stability of the intervention material before any vascular outcome is measured.

Human cardiovascular evidence

Table 3. Representative human evidence for lycopene and cardiovascular physiology

Evidence source	Design / population	Lycopene exposure	Cardiovascular interpretation
Gajendragadkar et al. [1]	Double-blind RCT; 36 CVD patients + 36 healthy volunteers; 2 mo	7 mg/d lycopene vs placebo	Endothelium-dependent vasodilatation improved by 53% in CVD patients; healthy volunteers showed no comparable response 15 mg/d improved SOD and DNA-damage endpoints; within-group RH-PAT increased, especially with lower baseline endothelial function
Kim et al. [2]	Randomized double-blind trial; 126 healthy men; 8 wk	6 or 15 mg/d vs placebo	Effects differed by endpoint; pooled evidence addressed lipids, BP, inflammation and endothelial function
Cheng et al. [3]	Systematic review/meta-analysis; 21 intervention studies	Tomato products and/or lycopene	

Evidence source	Design / population	Lycopene exposure	Cardiovascular interpretation
Nam et al. [4]	2026 umbrella review; 9 systematic reviews, 7 with meta-analysis	Tomato-derived lycopene interventions	High-certainty evidence supported blood-pressure improvement; lipid-profile evidence was more heterogeneous

Gajendragadkar et al. randomized patients with established cardiovascular disease and healthy volunteers to 7 mg/day lycopene or placebo for two months. Endothelium-dependent vasodilatation improved by 53% in the cardiovascular-disease group, while the healthy arm showed no comparable response [1]. Kim et al. studied 6 or 15 mg/day in healthy men and reported greater SOD activity and lower DNA damage at 15 mg/day; endothelial indices improved most clearly among participants with lower baseline function [2].

The evidence syntheses broaden the endpoint range. Cheng et al. pooled 21 intervention studies and found different patterns for lipids, blood pressure, inflammation, and endothelial function [3]. A 2026 umbrella review by Nam et al. judged the blood-pressure evidence to be more consistent than the lipid-profile evidence [4]. Earlier meta-analyses by Ried and Fakler [5] and by Li and Xu [6] reported blood-pressure signals under selected conditions, whereas Tierney et al. emphasized heterogeneity across dose and delivery format [7].

Discussion

Endothelial function as a sensitive intermediate phenotype

Endothelial function can move without parallel changes in conventional risk factors. In the Gajendragadkar trial, endothelium-dependent vasodilatation changed while endothelium-independent vasodilatation, blood pressure, arterial stiffness, lipids, and hsCRP did not show the same pattern [1]. That separation is useful for trial design because it argues for choosing a primary vascular phenotype rather than expecting every cardiometabolic marker to shift together.

Blood pressure and lipid outcomes: evidence heterogeneity as biological information

Blood-pressure and lipid summaries differ partly because the trials differ. Baseline pressure, medication, tomato food versus purified supplement, dose, duration, and background diet all vary across the evidence base [3]-[7]. The practical implication is methodological: a formulation-specific study should select its primary endpoint before recruitment and enroll a population in which that endpoint has room to change.

Redox measurements can help explain a vascular response without being used as a proxy for it. Devaraj et al. found dose-dependent increases in plasma lycopene and changes in selected oxidative-DNA endpoints, while several lipid-peroxidation measures were less responsive [8]. Gärtner et al. demonstrated greater lycopene bioavailability from tomato paste than from fresh tomatoes [9], and Unlu et al. showed that a cis-isomer-rich processed tomato sauce could yield higher relative bioavailability than an all-trans-rich preparation [10].

Food-based interventions provide additional vascular context. Hadley et al. reported higher plasma lycopene and greater lipoprotein resistance to ex vivo oxidation after processed tomato products [11]. In type 2 diabetes, Upritchard et al. found that tomato juice increased plasma lycopene nearly threefold and increased LDL-oxidation lag time by 42% [12]. Engelhard et al. reported lower systolic and diastolic pressure during an 8-week antioxidant-rich tomato-extract phase in grade-1 hypertension, without a parallel lipid change [13].

Not every tomato intervention produces broad cardiometabolic improvement. In a randomized controlled trial of a tomato-rich diet, Thies et al. found no uniform improvement across the tested cardiovascular-risk markers in moderately overweight but otherwise disease-free adults [14]. More recently, Yoshida et al. randomized adults with borderline FMD to placebo, tomato juice, or high-lycopene tomato juice for 12 weeks. FMD was higher in both active groups at week 12, while measured

oxidative-stress markers did not differ between groups [15]. That endpoint separation is useful when selecting outcomes for the present lipid matrix.

Relevance of a stable lipid matrix

The NVTIA® oil resin contributes control over the intervention material. Total lycopene, all-trans proportion, peroxide value, sediment, and 30-day retention remained within narrow ranges across the three optimized formulations. A stable lipid phase reduces the chance that storage-related carotenoid loss or oil oxidation becomes an unmeasured source of exposure variability.

Isomer preservation and cardiovascular translation

All-trans preservation documents process integrity, but isomer distribution after ingestion is a separate question. Processed tomato matrices increase circulating lycopene, and human studies show substantial postabsorptive cis-isomer representation. Plasma total lycopene and isomer distribution should therefore be measured alongside vascular outcomes rather than inferred from the starting oil composition.

Study Considerations and Future Directions

A direct study can recruit participants with a defined vascular phenotype, such as borderline flow-mediated dilation or elevated-normal blood pressure. Serial plasma lycopene/isomer measurements can be paired with FMD or RH-PAT, standardized blood pressure, oxidized LDL, hsCRP, and selected adhesion markers. The primary endpoint and medication background should be prespecified.

Conclusion

The high-stability lycopene oil formulations contained 2.13-2.34% total lycopene, 85.1-86.2% all-trans lycopene, low peroxide values, and retained 90.8-91.6% of total lycopene after 30 days at 45°C. Human evidence shows endpoint- and population-dependent cardiovascular responses, with endothelial and blood-pressure signals appearing more consistently than some lipid outcomes. The formulation provides a reproducible lycopene exposure for vascular studies that measure circulating carotenoid status and a defined cardiometabolic phenotype in the same protocol.

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