

Article

Stability-Preserved Lycopene in a Low-Oxygen Lipid Matrix: Oxidative-Stress Biomarkers and Human Nutritional Relevance

Yassine Igoundaz¹, Preston Brooks², Derek Palmer³

1,2,3. National Laboratory of Medicine LLC

Citation: Igoundaz Y. Stability-Preserved Lycopene in a Low-Oxygen Lipid Matrix: Oxidative-Stress Biomarkers and Human Nutritional Relevance. American Journal Of Bioscience And Clinical Integrity 2026, 3(9), 8-13.

Received: 10th Jun 2026

Revised: 11th Jul 2026

Accepted: 24th Aug 2026

Published: 24th Sept 2026



Copyright: © 2026 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>)

Abstract: A low-oxygen lycopene lipid complex was characterized for extraction transfer, isomeric integrity, oil-phase quality, and accelerated stability. The three optimized formulations transferred 78.2-82.1% of lycopene from the processed peel material, contained 2.13-2.34% total lycopene, and retained 85.1-86.2% in the all-trans form. After 30 days at 45°C under nitrogen and light protection, total lycopene retention remained 90.8-91.6%; ABTS capacity retained 89.8-90.8% of baseline. Human lycopene studies show endpoint-specific redox responses rather than a uniform antioxidant effect. Purified lycopene has altered DNA-oxidation measures and superoxide dismutase activity in randomized trials, while tomato-food interventions have changed resistance of lipoproteins or lymphocytes to experimental oxidation. The formulation data define a chemically stable starting material for human studies in which circulating lycopene, isomer distribution, and a small prespecified redox-biomarker panel are measured together.

Keywords: lycopene; oxidative stress; carotenoids; antioxidant defense; all-trans lycopene; lipid matrix; tomato; NVTIA®

Introduction

Lycopene is highly unsaturated and readily affected by oxygen, light, and heat. The conjugated double-bond system that gives the carotenoid its redox chemistry also makes processing conditions important. Before a biological response can be interpreted, the finished ingredient needs a defined lycopene concentration, isomer profile, and oil-phase oxidation state.

Randomized human work has not produced the same response for every oxidative-stress marker. Devaraj et al. found the clearest DNA-oxidation changes at the higher purified-lycopene dose [1]. Kim et al. reported increased plasma SOD activity and lower lymphocyte DNA damage at 15 mg/day [2]. The meta-analysis by Chen et al. found a pooled effect for comet-assay DNA tail length but not for LDL-oxidation lag time [3]. This endpoint selectivity makes formulation quality and exposure measurement particularly useful.

The NVTIA® process uses moderate-temperature enzymatic disruption, ethanol replacement dehydration, deoxygenated lipid extraction, cyclic enrichment, cold precipitation, and vacuum devolatilization. We examined whether those steps retained lycopene and oil quality, then compared the resulting exposure platform with human redox studies without treating external clinical results as outcomes of the present formulation.

Materials and Methods

Lycopene-rich tomato-peel matrix and low-oxygen enrichment

Tomato peel with seed content at or below 1.0% on a dry basis was adjusted to pH 4.4-5.0 and 58-70% moisture. Pectinase, cellulase, and hemicellulase treatment was performed at 40-46°C. Food-grade ethanol (75-90% v/v) was added after enzymatic treatment for termination and replacement dehydration, reducing moisture to 20-30%. The food-grade lipid phase contained 65-82% caprylic/capric triglyceride together with high-oleic sunflower oil, mixed tocopherols, and L-ascorbyl palmitate. Dissolved oxygen in the oil phase was controlled at ≤ 3.0 mg/L. Lycopene was enriched through 2-4 cyclic contacts at 40-50°C under light protection and a nitrogen-controlled headspace ($\leq 5\%$ oxygen).

Analytical characterization and stability

Total lycopene and geometric isomers were measured by C30 HPLC. Transfer rate was calculated from lycopene recovered in the final oil resin relative to the amount in cumulatively charged low-moisture tomato peel. Moisture, residual ethanol, and peroxide value were measured as product-quality variables. Accelerated stability was tested in amber glass under nitrogen at 45°C for 30 days. ABTS radical-scavenging capacity was recorded as an in-vitro storage-quality measurement in μmol Trolox equivalents per gram.

Human-evidence identification

Human evidence through August 2026 was reviewed for randomized interventions, systematic reviews/meta-analyses, and bioavailability studies relevant to DNA oxidation, antioxidant enzymes, lipid oxidation, circulating lycopene, and isomer handling. Human findings were used to select physiological endpoints and dose ranges; formulation data and external intervention data were kept separate.

Results

Transfer efficiency and compositional integrity

Table 1. Analytical quality of the three 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

Lycopene transfer into the final oil resin was 78.2-82.1% across the three optimized formulations. Total lycopene was 2.13-2.34%, and all-trans lycopene represented 85.1-86.2% of the measured pool. Moisture and residual ethanol remained low, with initial peroxide values of 1.8-2.0 mmol/kg.

Accelerated stability and antioxidant-related quality

Table 2. Accelerated storage performance of optimized 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

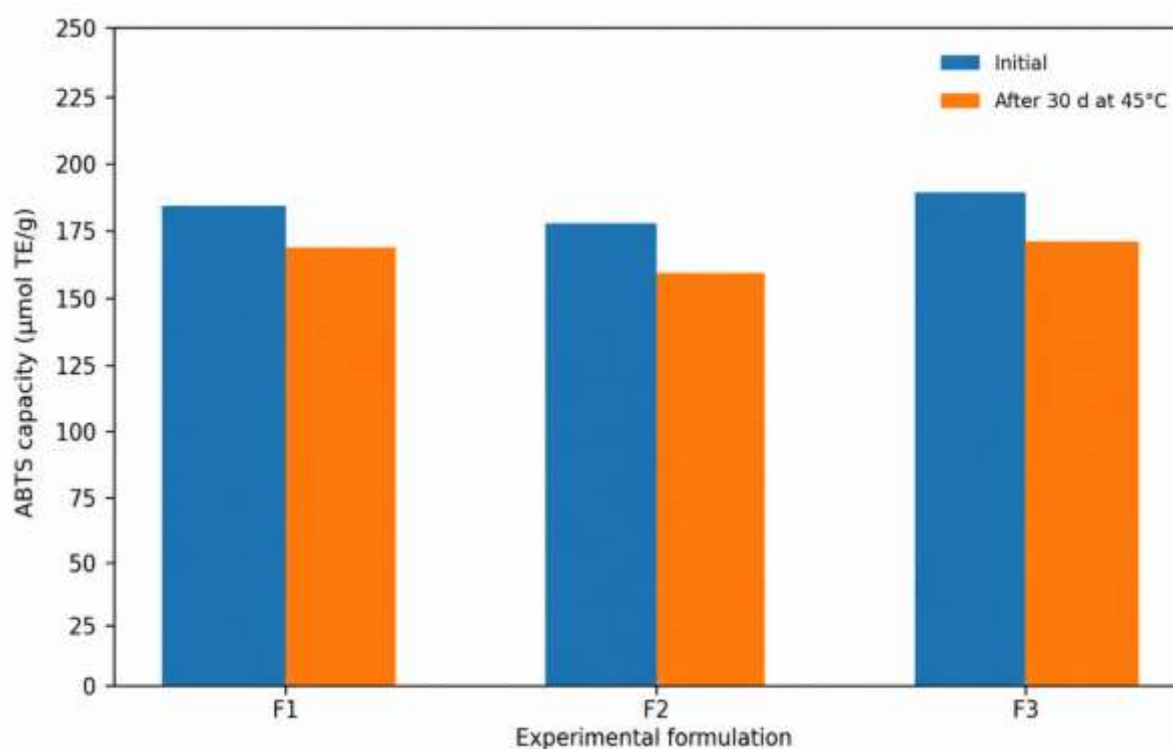


Figure 1. ABTS capacity of optimized formulations before and after 30 days of accelerated storage at 45°C. Values are direct analytical results; no error bars are added because replicate-level dispersion was not available for this endpoint.

After 30 days at 45°C, total lycopene retention was 91.6% for F1, 90.8% for F2, and 91.2% for F3. The all-trans proportion changed by -3.1, -2.9, and -3.3 percentage points. Sediment was 0.9%, 1.0%, and 0.8%, respectively, and all three samples remained uniform dark-red oily liquids. ABTS capacity retained 89.8-90.8% of baseline.

Human evidence for oxidative-stress responses**Table 3.** Representative human evidence linking lycopene intake with oxidative-stress biomarkers

Study	Population / design	Intervention	Key oxidative-stress observations
Devaraj et al. [1]	77 healthy adults ≥40 y; double-blind RCT; 8 wk	0, 6.5, 15, or 30 mg/d purified lycopene	30 mg/d reduced comet-assay DNA damage and urinary 8-OHdG; several lipid-peroxidation markers were unchanged
Kim et al. [2]	126 healthy men; randomized double-blind trial; 8 wk	Placebo, 6 mg/d, or 15 mg/d lycopene	15 mg/d increased SOD activity and reduced lymphocyte DNA comet-tail length versus placebo
Chen et al. [3]	Systematic review/meta-analysis of RCTs	Oral lycopene interventions	Pooled evidence suggested improvement in selected oxidative-stress biomarkers, with substantial endpoint heterogeneity
Hadley et al. [4]	60 healthy adults >40 y; randomized dietary intervention; 15 d	Processed tomato products providing ~23-35 mg/d lycopene	Plasma lycopene increased and lipoprotein resistance to ex vivo oxidative stress improved

Devaraj et al. randomized 77 adults aged at least 40 years to 0, 6.5, 15, or 30 mg/day purified lycopene for 8 weeks. The 30 mg/day dose reduced lymphocyte comet-assay DNA damage and urinary 8-OHdG, while several lipid-peroxidation measures were unchanged [1]. In 126 healthy men, Kim et al. found that 15 mg/day increased SOD activity and reduced lymphocyte DNA comet-tail length relative to placebo [2]. Chen et al. summarized the broader randomized literature and reported improvement in selected oxidative-stress measures with substantial endpoint heterogeneity [3]. Hadley et al. provided a food-based comparison: processed tomato products increased plasma lycopene and resistance of lipoproteins to ex vivo oxidative stress [4].

Discussion**Why formulation stability matters for antioxidant nutrition**

The stability result is chemical. Lycopene content, all-trans proportion, peroxide value, sediment, and ABTS-related analytical quality remained tightly controlled in the optimized oil resin. Moderate-temperature processing, ethanol replacement of water, deoxygenated oil, nitrogen headspace, and oil-phase antioxidants each address a different route of carotenoid or lipid deterioration. This makes the final material more reproducible for exposure studies.

Linking analytical preservation to human physiology

Human redox outcomes are less uniform than the formulation measurements. DNA comet assays, urinary 8-OHdG, SOD activity, LDL-oxidation lag time, TBARS, and other markers describe different molecular compartments and turnover rates. Devaraj, Kim, Hadley, and the Chen meta-analysis therefore should not be compressed into a single 'antioxidant' endpoint [1]-[4].

Oil matrix, bioavailability, and isomer context

Food structure and lipid association affect exposure. Rao and Agarwal reviewed human evidence on tomato-product bioavailability and in-vivo antioxidant properties [5]. Gärtner et al. showed higher lycopene bioavailability from tomato paste than from fresh tomatoes [6]. Unlu et al. found greater relative bioavailability from a cis-isomer-rich tomato sauce than from an all-trans-rich sauce [7]. Chronic intake of lycopene-rich tomato juice or supplements increased plasma lycopene and related tomato carotenoids in the study by Paetau et al. [8].

Antioxidant-related quality as a translational bridge

The oil-resin ABTS result is best kept as a storage-quality indicator. Lycopene's singlet-oxygen-quenching chemistry is well established experimentally [9], and broader reviews describe the compound's food-matrix, isomer, and health literature [10]. Human physiological work should use circulating lycopene together with direct redox biomarkers rather than treating the in-vitro ABTS value as a clinical outcome.

Short food interventions give additional examples of biomarker specificity. Porrini and Riso reported increased plasma and lymphocyte lycopene together with greater lymphocyte resistance to oxidative DNA damage after tomato puree consumption [11]. Bub et al. found that tomato juice reduced plasma TBARS and increased LDL-oxidation lag time in healthy men, whereas other carotenoid-rich foods in the same intervention did not produce identical lipid-peroxidation changes [12]. In type 2 diabetes, Upritchard et al. reported a nearly threefold rise in plasma lycopene and a 42% increase in LDL-oxidation lag time during tomato-juice supplementation [13].

A controlled feeding study by Riso et al. found that spinach plus tomato intake increased resistance of lymphocyte DNA to oxidative stress, although the response did not map simply onto cell carotenoid concentrations [14]. Bub et al. later showed that tomato-juice effects on lipid peroxidation could differ by PON1 genotype in a randomized crossover study [15]. These studies are useful for designing a compact biomarker panel and for recording host variables that may alter response.

Study Considerations and Future Directions

A direct formulation study can quantify plasma total and isomer-specific lycopene after a defined serving of the oil complex. DNA oxidation, F₂-isoprostanes, oxidized lipoproteins, antioxidant-enzyme activity, or inflammatory redox markers can then be prespecified rather than assembled after the result is known. Baseline lycopene status and oxidative-stress burden are useful stratification variables.

Conclusion

The low-oxygen oil complex transferred 78.2-82.1% of peel lycopene into the final matrix, contained 2.13-2.34% total lycopene, and retained 90.8-91.6% after 30 days at 45°C. ABTS capacity retained 89.8-90.8%. Human intervention evidence shows measurable lycopene-related changes in some DNA, antioxidant-enzyme, and lipoprotein-oxidation endpoints, but not in every redox marker. The stable formulation is therefore suited to exposure-controlled studies that define the biomarker question in advance.

REFERENCES

- [1] S. Devaraj et al., "A dose-response study on the effects of purified lycopene supplementation on biomarkers of oxidative stress," *J. Am. Coll. Nutr.*, vol. 27, no. 2, pp. 267-273, 2008, doi: 10.1080/07315724.2008.10719699.
- [2] J. Y. Kim et al., "Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men," *Atherosclerosis*, vol. 215, no. 1, pp. 189-195, 2011, doi: 10.1016/j.atherosclerosis.2010.11.036.

- [3] J. Chen, Y. Song, and L. Zhang, "Effect of lycopene supplementation on oxidative stress: an exploratory systematic review and meta-analysis of randomized controlled trials," *J. Med. Food*, vol. 16, no. 5, pp. 361-374, 2013, doi: 10.1089/jmf.2012.2682.
- [4] C. W. Hadley, S. K. Clinton, and S. J. Schwartz, "The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidative damage," *J. Nutr.*, vol. 133, no. 3, pp. 727-732, 2003, doi: 10.1093/jn/133.3.727.
- [5] A. V. Rao and S. Agarwal, "Bioavailability and in vivo antioxidant properties of lycopene from tomato products and their possible role in the prevention of cancer," *Nutr. Cancer*, vol. 31, no. 3, pp. 199-203, 1998, doi: 10.1080/01635589809514703.
- [6] C. Gärtner, W. Stahl, and H. Sies, "Lycopene is more bioavailable from tomato paste than from fresh tomatoes," *Am. J. Clin. Nutr.*, vol. 66, no. 1, pp. 116-122, 1997, doi: 10.1093/ajcn/66.1.116.
- [7] N. Z. Unlu, T. Bohn, D. M. Francis, H. N. Nagaraja, S. K. Clinton, and S. J. Schwartz, "Lycopene from heat-induced cis-isomer-rich tomato sauce is more bioavailable than from all-trans-rich tomato sauce in human subjects," *Br. J. Nutr.*, vol. 98, no. 1, pp. 140-146, 2007, doi: 10.1017/S0007114507685201.
- [8] I. Paetau et al., "Chronic ingestion of lycopene-rich tomato juice or lycopene supplements significantly increases plasma concentrations of lycopene and related tomato carotenoids in humans," *Am. J. Clin. Nutr.*, vol. 68, no. 6, pp. 1187-1195, 1998, doi: 10.1093/ajcn/68.6.1187.
- [9] P. Di Mascio, S. Kaiser, and H. Sies, "Lycopene as the most efficient biological carotenoid singlet oxygen quencher," *Arch. Biochem. Biophys.*, vol. 274, no. 2, pp. 532-538, 1989.
- [10] E. N. Story, R. E. Kopec, S. J. Schwartz, and G. K. Harris, "An update on the health effects of tomato lycopene," *Annu. Rev. Food Sci. Technol.*, vol. 1, pp. 189-210, 2010, doi: 10.1146/annurev.food.102308.124120.
- [11] M. Porrini and P. Riso, "Lymphocyte lycopene concentration and DNA protection from oxidative damage is increased in women after a short period of tomato consumption," *J. Nutr.*, vol. 130, no. 2, pp. 189-192, 2000, doi: 10.1093/jn/130.2.189.
- [12] A. Bub et al., "Moderate intervention with carotenoid-rich vegetable products reduces lipid peroxidation in men," *J. Nutr.*, vol. 130, no. 9, pp. 2200-2206, 2000, doi: 10.1093/jn/130.9.2200.
- [13] J. E. Upritchard, W. H. Sutherland, and J. I. Mann, "Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes," *Diabetes Care*, vol. 23, no. 6, pp. 733-738, 2000, doi: 10.2337/diacare.23.6.733.
- [14] P. Riso et al., "Spinach and tomato consumption increases lymphocyte DNA resistance to oxidative stress but this is not related to cell carotenoid concentrations," *Eur. J. Nutr.*, vol. 41, no. 3, pp. 95-100, 2002, doi: 10.1007/s003940200014.
- [15] A. Bub, S. W. Barth, B. Watzl, K. Briviba, and G. Rechkemmer, "Paraoxonase 1 Q192R (PON1-192) polymorphism is associated with reduced lipid peroxidation in healthy young men on a low-carotenoid diet supplemented with tomato juice," *Br. J. Nutr.*, vol. 93, no. 3, pp. 291-297, 2005, doi: 10.1079/BJN20041309.