Review

Lycopene: Implications for Human Health–A Review

Lynda M. Doyle, MS, MBA*

Human Nutrition, Avant Nutrition, LLC, Rockaway, NJ 07866, USA

*Corresponding author
Lynda M. Doyle, MS, MBA
President and CEO, Human Nutrition, Avant Nutrition, LLC, Rockaway, NJ 07866, USA; E-mail: lyndamdoyle@gmail.com

ABSTRACT

Lycopene is one of the six major dietary and serum carotenoids, and a potent antioxidant and anti-inflammatory agent. A large and growing body of scientific evidence supports the role of lycopene in multiple areas of health, including cancer, prostate, cardiometabolic, lung, skin, and liver health, and elucidates lycopene's mechanisms of action. This paper provides an overview of several benefit areas, specifically prostate, testes, cardiovascular, liver and skin health.

Keywords
Lycopene; Carotenoids; Cardiovascular disease (CVD); Human health.

INTRODUCTION

Carotenoids are naturally occurring, generally fat-soluble pigments synthesized by plants, algae, and photosynthetic bacteria. Over 750 carotenoids are found in nature and 1,117 are catalogued in the Carotenoids Database. Carotenoids are responsible for the yellow, orange, and red colors in nature. Of the 40-50 carotenoids found in the human diet, lycopene is among the 6 most common dietary carotenoids, including α-carotene, β-carotene, β-cryptoxanthin, lutein, and zeaxanthin. These are grouped into provitamin A carotenoids (α-carotene, β-carotene, β-cryptoxanthin) and non-provitamin A carotenoids (lycopene, lutein, and zeaxanthin). Lycopene contains 11 conjugated double bonds and undergoes cis-trans isomerization through light, thermal energy and chemical reactions.

Lycopene is present in orange-red fruits and vegetables, such as tomatoes, papayas, red peppers, pink grapefruit, and watermelons. The highest natural concentration is found in gac fruit, from a tropical vine in Southeast Asia. Tomatoes and tomato-based products, such as ketchup, tomato juice, tomato paste and tomato sauce, provide at least 80% of dietary lycopene in western countries such as the United States. The average daily consumption of lycopene in the western world is 5-7 mg. Lycopene from highly processed tomatoes is more bioavailable than that from raw tomatoes. Cooking and processing help release the lycopene from its plant matrix and convert lycopene from its natural straight (trans) structure to a more bioavailable geometric (cis) isomer because lycopene is fat soluble, dietary fat improves absorption.

Since the human body cannot synthesize lycopene, it must be consumed in the diet or taken as a dietary supplement. A significant portion of intact lycopene is absorbed by humans, which circulates through and accumulates in the liver, plasma and other tissues. Lycopene is first emulsified and solubilized into micelles before absorbed into the intestinal mucosa, then transported with other dietary lipids via chylomicrons through the lymphatic system to the blood. Lycopene is the most predominant carotenoid in the plasma and concentrates in low-density and very-low-density lipoprotein fractions of serum due to its lipophilic nature. Lycopene is found in most human tissues with preferential accumulation in the testes, adrenal glands, liver and prostate.

Major health problems nowadays deal with the accumulation of reactive oxygen species (ROS) accompanied with abnormalities, such as inflammation and irregular lipid metabolism, that are the primary risk factor for the increased prevalence of lifestyle metabolic diseases. ROS, also called free radicals, are highly reactive, unstable molecules that contain oxygen, and a build-up of these may cause damage to deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and proteins, and ultimately may cause cell death. With 11 conjugated double bonds, lycopene is one of the most potent antioxidants and free radical scavengers with stronger antioxidant properties than other serum carotenoids. Lycopene has the highest singlet oxygen quenching rate of the carotenoids, specifically twice that of β-carotene and 10 times greater than...
α-tocopherol.26,27 By reducing the burden of ROS and oxidative stress, lycopene has been shown to prevent oxidative damage to lipids, proteins and cells.5,38

**PROSTATE HEALTH**

Prostate cancer is the second most frequently diagnosed cancer in men globally and the fifth leading cause of death worldwide.29 In the United States, after skin cancer, prostate cancer is the second most common cancer in men, accounting for 9.5% of all new cancer cases.30,31 The primary risk factors are obesity, age, and family history. Positive prostate health outcomes have been asso- 

ciated with dietary intake of tomatoes, tomato-based products and lycopene supplementation, and lycopene blood levels.32-35 In a dose-response meta-analysis of lycopene and prostate cancer research, Chen, et al demonstrated that higher lycopene con-

Table 1. Recent Studies - Lycopene and Prostate/Testes

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Lycopene Dose</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aly H et al.36</td>
<td>Male Wistar rats, 4mg/kg bw, 16 days</td>
<td>Significant prevention of - Testes weight reduction - in sperm count, motility, viability and daily sperm production - activation of Caspase-3 and -9</td>
<td></td>
</tr>
<tr>
<td>Nouri M et al.37</td>
<td>44 infertile men, 25mg lycopene, 12 weeks</td>
<td>Lycopene group significant ↑ total sperm count and concentration (p&lt;0.05) Within group significant ↑ ejaculate volume, total sperm count, concentration and motility Significant ↓ TAC (p&lt;0.05)</td>
<td></td>
</tr>
<tr>
<td>Tripathy A et al.38</td>
<td>Adult proven-fertile male Wistar rats, 1.5mg/0.5ml Tween-80/100g bw/d 30 days</td>
<td>Significant recovery in - Sperm count and motility, HOS tail-coiled spermatozoa (p&lt;0.001) - Testicular Δ5, 3β-HSD, 17β-HSD activities (p&lt;0.05) - Catalase (p=0.02 in testis, p=0.05 in sperm) - SOD (p=0.05 in testis and sperm) - CD, MDA (p=0.02) - Testicular cholesterol (p=0.05) - Serum testosterone (p&lt;0.05) - Gene expression of testicular androgenic enzymes (Δ5 &amp; 3β-HSD p=0.02, 17β-HSD p=0.05) - SOD, SGPT (p&lt;0.05)</td>
<td></td>
</tr>
<tr>
<td>Xu Q et al.39</td>
<td>Male Wistar rats, 4mg/kg bw, 60 days</td>
<td>Inhibited BaP-caused decrease in sperm motility and concentration, increase in head, tail and total abnormal sperm rate ↓ MDA, ROS, TBARS ↑ GPx, GSH/GSSG, CAT, SOD</td>
<td></td>
</tr>
<tr>
<td>Beynon RA et al.40</td>
<td>133 human men 50-69 years with elevated PSA, 15mg capsules, blinded, lycopene-rich foods, unblinded, 6 months</td>
<td>↓ Circulating pyruvate (higher levels linked to higher PCA risk)</td>
<td></td>
</tr>
<tr>
<td>Jiang L et al.41</td>
<td>Male mice, 0, 1, 5, or 10 mg/kg</td>
<td>Significant improvement (p&lt;0.01) in survival rate Significant ↓ tumor volume (p&lt;0.001) all doses ↓ in serum inflammatory markers (IL1, IL6, IL8, and TNF-α) dose dependent</td>
<td></td>
</tr>
<tr>
<td>Lane JA et al.42</td>
<td>133 human men 50-69 years with elevated PSA, 15mg capsules, blinded, lycopene-rich foods, unblinded, 6 months</td>
<td>↑ mean lycopene 1.28x higher in capsule and 1.42x higher in food than placebo</td>
<td></td>
</tr>
</tbody>
</table>

Male Infertility

Infertility affects an estimated 70 million people globally,46 where male infertility contributes to 50% of the cases, according to the World Health Organization (WHO). Evidence suggests that oxidative stress caused by excessive amounts of ROS plays a role in idiopathic male infertility.47 This results in sperm membrane lipid peroxidation, DNA damage, and apoptosis leading to decreased sperm viability and motility.48 Lycopene concentration in testes is significantly lower in infertile men.49 Supplementation has been shown to increase seminal plasma lycopene,40 and lycopene may increase ROS and cancer cell proliferation, thus causing somatic DNA mutations and increased angiogenesis.50 In addition to its ability to quench free radicals, lycopene may reduce the risk of prostate cancer by additional mechanisms. Lycopene impacts intercellular communication modulation and the alteration of intracellular signaling pathways,42 which include an upregulation in intercellular gap junctions,43 an increase in cellular differentiation,40 and alterations in phosphorylation of some regulatory proteins.41 Physiological concentrations of lycopene have been shown to inhibit cell line proliferation in combination with α-tocopherol42 and lycopene was shown to inhibit prostate cancer cell proliferation via PPAR-LXRα-ABCA1 pathway.51 Lycopene attenuates the risk of prostate cancer by modulating the expression of growth and survival associated genes, e.g. CDK7, BCL2, EGFR, and IGF-1R.52 Multiple lycopene doses showed significant improvement in survival rate of and significant reduction of tumor volume in mice injected with prostate cancer cell lines.53 Oxidative stress plays a role in prostate cancer by in-
play a role as an antioxidant in the process of spermatogenesis.  

Multiple lycopene supplementation studies have shown promising results in reducing male infertility in both human and animal models. Results include a decrease in lipid peroxidation and DNA damage, an increase in sperm count and viability, and general immunity. Lycopene has been shown to reduce lipid peroxidation. Lycopene increases sperm count and concentration and a significant increase in transient aplastic crisis (TAC) (Table 1). Supplementation over 12-weeks in infertile men resulted in a significant increase in docosahexaenoic acid (DHA)/arachidonic acid (AA) ratio in seminal plasma. Daily supplementation of 4-8 mg lycopene improves sperm motility, which was also shown in animal studies. Daily supplementation with 14 mg lactolycopene, a combination of lycopene with whey protein, was shown to improve sperm motility and morphology in young healthy men. Durairajanayagam et al concluded that daily 4-8 mg lycopene supplementation for 3-12-months is sufficient to treat male infertility. Supplementation of 20 mg/d lycopene for 3-months prior to in vitro fertilization (IVF) treatment resulted in 7 spontaneous pregnancies prior to treatment and 15 pregnancies post treatment and a significant improvement in mitochondrial ROS, MAPKs, ANP, BNP, mitochondrial ROS, MAPKs, NO, MDA, GSH, GSH-Px, SOD, CAT, IgG (3 × serum lycopene by 2.9- and 4.3-fold after 2 and 4 weeks, respectively decreased serum lycopene levels, were shown to be strongly predictive of all-cause mortality and poor outcomes of CVD. Daily lycopene supplementation has been shown to increase serum lycopene concentration and reduce oxidative stress markers and improve antioxidant status.

Evidence suggests that Mediterranean countries have lower risks of CVD mortality when compared to other regions of Europe and the United States. This effect has been attributed to a diet rich in vegetables, including tomatoes, tomato products and olive oil. While low plasma levels of lycopene have been reported in hypertension, myocardial infarction, stroke, and atherosclerosis, dietary intake and high serum concentration of lycopene significantly reduced the risk of major cardiac events. In addition, epidemiological studies support the role of lycopene in the prevention of cardiovascular disease.

Oxidative stress plays a significant role in cardiovascular disease and may be a major cause of lycopene depletion in ageing and cardiovascular disease. Low carotenoid levels, especially decreased serum lycopene levels, were shown to be strongly predictive of all-cause mortality and poor outcomes of CVD. Daily lycopene supplementation has been shown to increase serum lycopene concentration and reduce oxidative stress markers and improve antioxidant status. Lycopene was shown to reduce the synthesis of AGE, inflammation, impaired monocyte-endothelium interaction, T-lymphocytes activation, synthesis of advanced glycation products (AGE) and their receptors (RAGE), and down-regulation of cyclooxygenase 2. Lycopene inhibited the expression of ICAM-1, TNF-α induced NFkB activation and interaction between monocytes and endothelial cells. Serum lycopene was inversely associated with VCAM-1 and LDL. Kim et al showed lycopene supplementation improved microvascular function, measured by decreased concentrations of sVCAM and sICAM, a reduction in DNA damage, and an increase in superoxide dismutase (SOD) activity.

Cardiovascular disease (CVD) is the leading cause of mortality worldwide. Key risk factors include high blood pressure, high cholesterol and smoking. Damage and remodeling of blood vessels can result in blood flow restrictions affecting the heart and central nervous system in CVD, and atherosclerosis is the leading cause of CVD.

### Table 2. Recent Studies - Lycopene and Cardiovascular Health

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Lycopene Dose</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdel-Daim MM et al.</td>
<td>56 Swiss albino mice</td>
<td>10mg, 15 days</td>
<td>↑ GSH, GSH-Px, SOD, CAT, IgG (3 × serum lycopene by 2.9- and 4.3-fold after 2 and 4 weeks, respectively)</td>
</tr>
<tr>
<td>Brito AK, et al.</td>
<td>30 male hamsters</td>
<td>25, 50mg lycopene-rich extract, 38 days</td>
<td>Significant ↑ TG, MDA-p, MDO</td>
</tr>
<tr>
<td>Kumar R et al.</td>
<td>24 male SD rats</td>
<td>50mg/kg, 45 days</td>
<td>Significant ↑ HDL-C (p&lt;0.05); ↑ TC, LDL-C, very LCL-C, TG</td>
</tr>
<tr>
<td>Petryaev IM et al.</td>
<td>142 human adults with coronary vascular disease</td>
<td>7mg either lycopene-rich extract or lycopene-formulated GA lycopene (LYC), 4 wks</td>
<td>LYP ↑ serum lycopene by 2.9- and 4.3-fold after 2 and 4 weeks; LAC by 0.5-fold after 4 weeks</td>
</tr>
<tr>
<td>Saracoglou G et al.</td>
<td>Wistar albino STZ rats</td>
<td>4mg/kg, 28 days</td>
<td>↑ GPx, SOD, CAT, MDA</td>
</tr>
<tr>
<td>Yilmaz S et al.</td>
<td>42 male Wistar albino rats</td>
<td>5mg/kg, 15 days</td>
<td>↑ GSH, GST, GSH-Px, SOD, CAT, Ge6PD, MDA</td>
</tr>
<tr>
<td>Zeng J et al.</td>
<td>C57BL6j mice</td>
<td>50mg/kg, 5 wks</td>
<td>↑ Inhibited cardiac hypertrophy and improved cardiac dysfunction, ↓ ANP, BNP, ↓ mitochondrial ROS, MAPKs, ↓ HO-1, SOD1, CAT</td>
</tr>
<tr>
<td>Zheng Z et al.</td>
<td>T2DM rats</td>
<td>0, 5, 10, 15mg/kg Lycopene, 10 wks</td>
<td>Dose dependent ↑ oxidative stress markers (GHB, ox-LDL, and MDA) and inflammatory factors (TNF-α and CRP), ↑ TAC (CAT, SOD, and GPx)</td>
</tr>
</tbody>
</table>
down regulating their receptors (RAGE) which contributes to vessel protection. Lycopene reduced inflammatory markers in various animal models. Lycopene improves endothelial function by increasing the bioavailability of nitric oxide (NO), improving endothelium-dependent vasodilation, reducing protein, lipids, DNA and mitochondrial damage and increasing antioxidant potential. Lycopene supplementation reduced DNA damage, up-regulated mitochondrial gene expression and reduced mitochondrial oxidation. Foot-and-mouth disease (FMD) was significantly increased by 1.1 points (10.9%) with 4-weeks lycopene supplementation in individuals with stage 1 hypertension, who were otherwise healthy. Blood pressure was reduced with lycopene supplementation in individuals with stage 1 hypertension, who were otherwise healthy. Lycopene impacts blood lipids, where a dose-dependent reduction in intracellular cholesterol was seen in human studies, and lycopene and tomato products decreased plasma total cholesterol, low-density lipoprotein (LDL) cholesterol and increased high-density lipoprotein (HDL) cholesterol in animal models. Lycopene supplementation reduced cholesterol and LDLa in healthy postmenopausal women. Significant increase in HDL and decrease in total cholesterol (TC), LDL and triglyceride (TG) were observed in lycopene-supplemented rats, and a reduction in oxidized LDL in lycopene-supplemented humans and lycopene-supplemented rats.

Intima media thickness (IMT) is an established index of the structural change of an artery and IMT, especially that of the carotid, is associated with the presence of cardiovascular risk factors. Serum carotenoid and lycopene levels are inversely associated with intima-media thickness. Lycopene and lutein supplementation (20 mg each) resulted in a decrease in IMT after 12-months, where the combination proved more effective compared to lutein alone (Table 2).

LIVER HEALTH

The liver is the largest visceral organ in the abdominal cavity and largest gland in the body, weighting about 1.5 kg in a healthy adult. The liver plays a major role in metabolism, including the production of certain proteins, cholesterol and the conversion of excess glucose to glycogen, and is involved in over 500 vital functions such as drug detoxification, the production of bile and the synthesis of steroid hormones. Non-alcoholic fatty liver disease (NAFLD), the most common form of liver disease, refers to a group of conditions resulting in excess fat in the liver (hepatic steatosis) of people who drink little or no alcohol and involves the development of insulin resistance, lipid peroxidation, oxidative stress and inflammation. Global and US prevalence of NAFLD are both estimated at 24%. As potent antioxidants and anti-inflammatory agents, carotenoids can play a role in protecting the liver against oxidative stress, insulin resistance and inflammation. In a prospective study of Chinese adults aged 40-75-years, higher serum carotenoid concentrations were positively associated with NAFLD improvements, specifically in lowering serum RBP4, triglycerides, homeostasis model assessment-insulin resistance (HOMA-IR), and body mass index (BMI). Lycopene is one of the most studied carotenoids regarding NAFLD due to multiple mechanisms beyond its antioxidant capacity, such as regulation of gene expression and gap junctions, antiproliferative capacity, lipid peroxidation and immune and hormonal modulation.

Numerous animal models demonstrated a reduction in hepatic steatosis, reduced hepatic inflammation reduced lipid peroxidation and antioxidant protection. In a study with Sprague-Dawley rats, lycopene and tomato extract resulted in a significant decrease in cyto-

<table>
<thead>
<tr>
<th>Table 3. Recent Studies - Lycopene and Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors</strong></td>
</tr>
<tr>
<td>Bandeira ACB et al. 116</td>
</tr>
<tr>
<td>Karaca A et al. 131</td>
</tr>
<tr>
<td>Li C-C et al. 127</td>
</tr>
<tr>
<td>Sadek K et al. 128</td>
</tr>
<tr>
<td>Shimiw Y et al. 126</td>
</tr>
<tr>
<td>Wang J et al. 125</td>
</tr>
<tr>
<td>Yn Y et al. 79</td>
</tr>
</tbody>
</table>
Carotenoids accumulate in the skin and can protect against UV-generated ROS. Multiple factors impact their skin concentration. Dietary supplementation can increase skin carotenoid concentration, and oxidative stress, for example from cigarette smoking or exposure to UV-rays, can decrease their concentration. Lycopene skin and plasma concentration was shown to be comparable or higher than that of β-carotene. Lycopene supplementation increases both skin and plasma lycopene concentration, and a correlation between lycopene skin and plasma concentration has been demonstrated. Ribaya-Mercado et al found Lycopene to be the most quickly depleted antioxidant in skin upon solar radiation exposure, and suggest lycopene plays a role in mitigating photo-oxidative damage in tissues through protection against UV-radiation. A significant correlation between skin roughness and lycopene skin concentration has been seen.

Consumption of lycopene and lycopene-rich products protects the skin against sunburn by increasing the basal defense against UV light-mediated damage. Studies have demonstrated supplementation with lycopene or lycopene-rich products, or lycopene mixed with other carotenoids or antioxidants reduce UV-induced erythema and increase minimal erythema dose (MED). Forty percent (40%) reduction in erythema resulted after 10 weeks daily consumption of 40 g tomato paste, equivalent to 16 mg lycopene. Twelve weeks daily supplementation of 8 mg each of lycopene, lutein and β-caroteneameliorates UV-induced erythema. An increase in MED and reduction in UV-induced erythema was observed after 7-weeks daily supplementation of an antioxidant complex including lycopene, β-carotene, α-tocopherol and selenium. Lycopene-enriched tomato extract suppressed skin tumorigenesis in BALB/c mice, inhibited cell proliferation, decreased expression of angiogenic genes and increased expression of transmembrane proteins.

Lycopene protects the skin against photaging by its antioxidative capacity, anti-inflammatory effects, impact on gene expression, and protection against lipid peroxidation.

### Table 4. Recent Studies - Lycopene and Skin

<table>
<thead>
<tr>
<th>Authors</th>
<th>Population</th>
<th>Lycopene Dose, Duration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grether-Beck S et al.</td>
<td>65 healthy human adults</td>
<td>10 mg daily, 12 weeks</td>
<td>Inhibited mRNA expression of HO-1, MMP-1 and ICAM-1</td>
</tr>
<tr>
<td>Groten K et al.</td>
<td>149 healthy human adults</td>
<td>15 mg lycopene, 5.8 mg phytoene and phytofluene, 0.8 mg beta-carotene, 5.6 mg tocoferols from tomato extract and 4 mg carnosic acid from rosemery or placebo</td>
<td>Protected against UVB-induced erythema, Significantly ↓ UVB-induced IL6 and TNFα, ↑ plasma carotenoid levels</td>
</tr>
<tr>
<td>Koul A et al.</td>
<td>60 male Balb/c mice</td>
<td>5 mg/kg bw lycopene-enriched tomato extract</td>
<td>↓ tumor incidence, size, number, burden and volume, ↓ mRNA and protein expression of VEGF, Ang-2, bFGF, ↑ Cx-32, Cx-43</td>
</tr>
<tr>
<td>Petsev I et al.</td>
<td>32 healthy human adults</td>
<td>7 mg daily, 4 weeks</td>
<td>Significant ↑ serum concentration 2.6 &amp; 3.4x over control after 2 &amp; 4 wks, respectively, Stepwise ↑ in IF staining of skin corneocytes and sebum</td>
</tr>
<tr>
<td>Petsev I et al.</td>
<td>120 healthy human adults; subgroup for supplementation 15 healthy human adults</td>
<td>7 mg daily, 4 weeks</td>
<td>↑ Skin and serum lycopene concentration, Significant ↑ in desquamated corneocytes lycopene concentration during whole supplementation period, ↑ in sebum lycopene concentration during first 2 weeks of supplementation</td>
</tr>
</tbody>
</table>

**SKIN HEALTH**

The skin is the largest organ of the body, accounting for approximately 15% of total body weight. The skin protects against external physical, chemical, and biological assailants, prevents excess water loss from the body, and regulates body temperature. Carotenoids are essential for skin health as they protect against oxidative stress, fatty infiltration and necrosis caused by thermally oxidized tallow in a rat model. In a tramadol-induced hepatotoxicity rat model, lycopene reduced fatty acid degeneration and necrosis, and lipid peroxidation, inhibited DNA fragmentation and apoptosis signaling, and increased antioxidant and mitochondrial dysfunction in the mouse brain and liver. In a BCO1−/−/BCO2−/− double knockout mouse model, Li et al found Lycopene to be the most quickly depleted antioxidant in skin upon solar radiation exposure, and suggest lycopene plays a role in mitigating photo-oxidative damage in tissues through protection against UV-radiation. A significant correlation between skin roughness and lycopene skin concentration has been seen.

The skin is the largest organ of the body, accounting for approximately 15% of total body weight. The skin protects against external physical, chemical, and biological assailants, prevents excess water loss from the body, and regulates body temperature. Carotenoids are essential for skin health as they protect against oxidative stress, fatty infiltration and necrosis caused by thermally oxidized tallow in a rat model. In a tramadol-induced hepatotoxicity rat model, lycopene reduced fatty acid degeneration and necrosis, and lipid peroxidation, inhibited DNA fragmentation and apoptosis signaling, and increased antioxidant and mitochondrial dysfunction in the mouse brain and liver. In a BCO1−/−/BCO2−/− double knockout mouse model, Li et al demonstrated protective effects of lycopene against NAFLD in rats. Wang et al showed 5 weeks supplementation of 0.03% w/w lycopene added to chow ameliorated lipopolysaccharide (LPS)-induced insulin resistance and mitochondrial dysfunction in the mouse brain and liver. Li et al demonstrated 24-weeks of supplementation of 2.3 mg lycopene from tomato powder reduced the severity of hepatic steatosis, increased SIRT1, significantly increased lipogenesis and fatty acid oxidation, and reduced inflammation. Lycopene improved redox imbalance, increased antioxidant enzymes, and decreased inflammation, attenuating the effects of APAP-induced liver injury in mice (Tabel 3).

Carotenoids accumulate in the skin and can protect against UV-generated ROS. Multiple factors impact their skin concentration. Dietary supplementation can increase skin carotenoid concentration, and oxidative stress, for example from cigarette smoking or exposure to UV-rays, can decrease their concentration. Lycopene skin and plasma concentration was shown to be comparable or higher than that of β-carotene. Lycopene supplementation increases both skin and plasma lycopene concentration, and a correlation between lycopene skin and plasma concentration has been demonstrated. A significant correlation between skin roughness and lycopene skin concentration has been seen.

Consumption of lycopene and lycopene-rich products protects the skin against sunburn by increasing the basal defense against UV light-mediated damage. Studies have demonstrated supplementation with lycopene or lycopene-rich products, or lycopene mixed with other carotenoids or antioxidants reduce UV-induced erythema and increase minimal erythema dose (MED). Forty percent (40%) reduction in erythema resulted after 10 weeks daily consumption of 40 g tomato paste, equivalent to 16 mg lycopene. Twelve weeks daily supplementation of 8 mg each of lycopene, lutein and β-caroteneameliorates UV-induced erythema. An increase in MED and reduction in UV-induced erythema was observed after 7-weeks daily supplementation of an antioxidant complex including lycopene, β-carotene, α-tocopherol and selenium. Lycopene-enriched tomato extract suppressed skin tumorigenesis in BALB/c mice, inhibited cell proliferation, decreased expression of angiogenic genes and increased expression of transmembrane proteins.

Lycopene protects the skin against photaging by its antioxidative capacity, anti-inflammatory effects, impact on gene expression, and protection against lipid peroxidation.
Supplementation with lycopene-rich TNC and lutein-containing capsules resulted in a significant reduction of UV-induced mRNA expression of HO-1, MMP-1 and ICAM-1. Lycopene, \( \beta \)-carotene, \( \alpha \)-tocopherol, and selenium supplementation showed a reduction of UV-induced p53 expression, sun burn cells (SBCs) and lipoperoxide levels. \[146\] Lycopene from tomato extract protected against upregulation of proinflammatory cytokines. \[7\] Supplementation of a lycopene, \( \beta \)-carotene and antioxidant combination inhibited the expression of matrix metalloproteinase (Table 4). \[148\]

## CONCLUSION

Lycopene, one of the six most predominant carotenoids found in the human diet and plasma, is the most potent singlet oxygen quenching carotenoid and a strong anti-inflammatory agent. Aging and major health problems today deal with the accumulation of ROS, including inflammation and irregular lipid metabolism. Due to its antioxidative and anti-inflammatory effects, and other mechanisms demonstrated in the research, for example lipid metabolism and cellular communication and differentiation, lycopene can play a protective role in aging and be a key component in strategies to tackle lifestyle metabolic and chronic health issues.

## REFERENCES

14. Unlu, NZ; Bohn, T; Clinton, SK; Schwartz, SJ. Carotenoid absorption from salad and salsa by humans is enhanced by the addition of avocado or avocado oil. *J Nutr.* 2005; 135(3): 431-436. doi: 10.1093/jn/135.3.431


46. Fainberg J, and Kashanian, A. Recent advances in understand-


96. Engelhard YN, Gazer B, Paran E. Natural antioxidants from...


103. Lind L. Flow-mediated vasodilation was found to be an independent predictor of changes in the carotid plaque status during a 5-year follow-up. J Atheroscler Thromb. 2014; 21: 161-168. doi: 10.5551/jat.18572


