Tomato carotenoids supplementation: Photo-protection and skin anti-aging activity

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Photooxidative Stress

UV LIGHT

Reactive Oxygen Species (ROS)

Antioxidants

Damage

DNA
LIPIDS PROTEINS
Photooxidative Stress - Problems of Sun-exposed skin

- Sunburn
- Skin Aging
- Skin Cancer
Tomato carotenoids and Skin Health

- Endogenous Photo protection
- Cosmetics: Skin structure and texture
- Protection against Sunburn Cell Formation
- Lycopene and protection from erythema
- Is it only lycopene?
- UV-A and UV-B
UV exposure during a conservative vacation accounts only for about 1/3 of the average erythemal UV doses within a year.
Endogenous Photoprotection

This presentation will address the concept of Photoprotection by dietary means.
Tomato carotenoids and Skin Health

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- Cosmetics: Skin structure and texture
- Protection against Sunburn Cell Formation
- Lycopene and protection from erythema
- Is it only lycopene?
- UV-A and UV-B
Antioxidant Supplements Improve Parameters Related to Skin Structure in Humans

U. Heinricha H. Tronniera W. Stahlb M. Béjotc J.-M. Maurettec

aInstitute of Experimental Dermatology, University of Witten/Herdecke, Witten, bInstitute of Biochemistry and Molecular Biology, University of Düsseldorf, Düsseldorf, Germany, and cLaboratoire Oenobiol, Paris, France
<table>
<thead>
<tr>
<th><strong>Parameters</strong></th>
<th><strong>Measurements</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>ultrasound</td>
</tr>
<tr>
<td>Thickness</td>
<td>(B-scan)</td>
</tr>
<tr>
<td>Scaling</td>
<td>Surface Evaluation</td>
</tr>
<tr>
<td>Roughness</td>
<td>of Living Skin (SELS)</td>
</tr>
<tr>
<td>Smoothness</td>
<td></td>
</tr>
<tr>
<td>Wrinkling</td>
<td></td>
</tr>
<tr>
<td>Hydration</td>
<td>Corneometry</td>
</tr>
<tr>
<td>Transepidermal</td>
<td></td>
</tr>
<tr>
<td>water loss</td>
<td>TEWL</td>
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</tbody>
</table>
Antioxidants mixture Vs. Placebo

6.0 mg Lycopene
4.8 mg ß-Carotene
10 mg α-Tocopherol
75 µg Selenium

(n= 13)
Duration: 12 wk;
measurements: wk=0, wk12
<table>
<thead>
<tr>
<th></th>
<th><strong>Treatment</strong></th>
<th></th>
<th><strong>Placebo</strong></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>wk 0</td>
<td>wk 12</td>
<td>wk 0</td>
<td>wk 12</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.68</td>
<td><strong>1.33</strong>*</td>
<td>0.46</td>
<td>0.46</td>
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<tr>
<td>Lycopene</td>
<td>0.52</td>
<td><strong>0.88</strong>*</td>
<td>0.49</td>
<td>0.60</td>
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<tr>
<td>α-Tocopherol</td>
<td>32.8</td>
<td>31.9</td>
<td>33.8</td>
<td>35.8</td>
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</table>
A typical ultrasound B-scan shows the density and thickness of the dermis.

Epidermis  Dermis  Subcutaneous

Dermis + Epidermis = Thickness of the skin

black areas are of low density

bright yellow are of high density

before

after 12 weeks
Difference wk 12 vs. wk 0

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density</td>
<td>+ 7% *</td>
<td>+0.3%</td>
</tr>
<tr>
<td>Thickness</td>
<td>+14% *</td>
<td>- 1.4%</td>
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</table>
Skin surface evaluation

White area show degree of **scaling**

Red area and steepness of peaks show **roughness** of skin

before after 12 weeks
## Difference wk 12 vs wk 0

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Scaling</td>
<td>- 60% *</td>
<td>- 30%</td>
</tr>
<tr>
<td>Roughness</td>
<td>- 33% *</td>
<td>- 16%</td>
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</table>
Mechanism ???

In a ongoing new study
A placebo controlled, double blind, cross-over study

Special emphasis on molecular markers of UVA damage in human volunteers

Performed by leading skin research university group in Europe
2. Assessment of skin barrier function / anti-aging by skin physiological parameters (measurement with bioengineering methods)
   a. Transepidermal water loss of the skin
   b. Skin elasticity
   c. Skin hydration
   d. Skin colour
   e. MED – Erythema
   f. PPD - Tanning
Study parameters

1. Molecular Parameters (skin biopsies):
   to be assessed by RT-PCR

- mRNA Expression of HO-1 (oxidative stress)
- ICAM-1 (skin irritation)
- MMP-1 (photoaging)
- Col1A1 and Col1A2 (skin rejuvenation)
- IL-1, IL-6 (skin inflammation)
Tomato carotenoids and Skin Health

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- UV-A and UV-B
Lyc-O-Mato® 6%
Dietary Supplementation Study
Protection against Sunburn Cell Formation
Sunburn cells, are apoptotic (dead) cells, which are indicative of damage caused by UV exposure.
Study Objective

Determination of the efficacy of oral supplementation of Lyc-O-Mato® in preventing photo-aging, as measured by the histological analysis of sunburn cells

Test Products

- Group 1 – Lyc-O-Mato® 6% capsules per day, (10 mg Lycopene)
- Group 2 – Placebo control capsules (containing Soybean oil)

Study Period

10 weeks of supplementation
Effect Of Dietary Supplementation Study-Cont’d

Study Population

- 10 female and male subjects, 18 + years of age, with skin Type I and II

Protocol

- Subjects were randomized into two balanced groups of five.
- Subjects returned the clinic at the end of week 10 for radiation of 2 MED.
- Subjects returned 24 hours later for 3mm punch biopsy for sunburn cell counts.
Number of Sunburn Cells per Sq. mm

After 10 weeks ingestion
In conclusion, Daily Dietary Supplementation can provide year round protection against UV radiation damage.
UV light and other forms of oxidative stress can modify the cellular genome by causing DNA damage and cell death.

What is the mechanism of tomato extract protection?
DNA damage after consumption of Lyc-O-Mato drink

Experimental design: double-blind, cross-over study,

**Carotenoid consumption per day:**
- 6 mg lycopene
- 4 mg phytoene
- 3 mg phytofluene
- 1 mg β-carotene
- 1.8 mg α-tocopherol,

Reduction in H$_2$O$_2$-induced DNA damage of human lymphocytes by Lyco-O-Mato drink

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Lycopene and other tomato carotenoids, in skin protection.

Wilhelm Stahl, Helmut Sies Institute for Physiological Chemistry I Heinrich-Heine-Universität, Düsseldorf, Germany
Irradiated Skin—Redness after 24h of UV-Exposure
Photoprotective Effects of Lycopene: Study Design

- 9 Volunteers (skin type II) ($\Delta$-a-Value at 1.25 MED)
- 40 g Tomato Paste/day = 16 mg Lycopene/day with olive oil
- 10 Week Supplementation
- Carotenoid Serum Levels (HPLC)
- Carotenoid Skin Levels (Chromametry)
- Erythema Formation (Sunburn Reaction)
  Chromametry: $\Delta$-a-Value

Results

- At week 10, erythema formation was 40% lower in the group that consumed tomato paste compared with controls.

Conclusion

Protection against UV light-induced erythema, can be achieved by ingestion of a commonly consumed dietary source of lycopene.
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Is it only lycopene?

UV-A and UV-B
Can lycopene alone replace the tomato?
Phytosterols 0.7%

Tocopherols (Vit E) 2%

Other carotenoids 0.3%

Phytofluene 0.7%

Phytoene 0.7%

Beta-carotene 0.2%

Lycopene 7%
Photoprotective Effects of Tomato Products vs Lycopene

- 36 Volunteers (skin type II)
- Synthetic Lycopene
  Lyc-O-Mato Capsules
  Lyc-O-Mato Drink
- 12 Week Supplementation
- Serum Levels of Lycopene, Phytoene, Phytofluene: HPLC
- Total carotenoid Skin Level (Reflection spectrophotometry)
- Erythema Formation ($\Delta$-a-Value at 1.25 MED)
  Sunburn Reaction to solar light simulator
# Carotenoid daily intake during the study

<table>
<thead>
<tr>
<th>Carotenoids (mg/d)</th>
<th>Lyc-O-Mato drink</th>
<th>Lyc-O-mato capsules</th>
<th>Lycopene synthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lycopene</td>
<td>8.2</td>
<td>9.8</td>
<td>10.2</td>
</tr>
<tr>
<td>Phytoene</td>
<td>4.5</td>
<td>1.0</td>
<td>-</td>
</tr>
<tr>
<td>Phytofluene</td>
<td>3.2</td>
<td>0.9</td>
<td>-</td>
</tr>
</tbody>
</table>
The combination of lycopene with other tomato carotenoid is more protective than synthetic lycopene.
The longer you consume the better protection you get.

Why Phytofluene and Phytoene are so beneficial?
Mechanism ???
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Phytofluene and Phytoene absorb light in UV-A and UV-B.

The graph shows the absorbance of Phytoene, Phytofluene, and Lycopene across different wavelengths. UV-B, UV-A, and the visible spectrum are indicated.

Absorbance

Wavelength (nm)

250 300 350 400 450 500
Phytofluene and Phytoene Features & Benefits:

- **Major carotenoids in tomatoes and in tomato extracts** (not present in synthetic preparations)
- **Absorb UV-A and UV-B** respectively
- **Both are colorless carotenoids**
Most sun care products provide optimal protection from UV-B, but incomplete protection from UV-A
Phytoene and Phytofluene as well as other tomato phyto-nutrients:

May provide the additional protection against the damaging oxidative free radicals
Mechanism ???

Erythema is inflammation
INFLAMMATION

The Secret Killer
The surprising link between INFLAMMATION and HEART ATTACKS, CANCER, ALZHEIMER’S and other diseases

READ THE STORY
What may be the mechanisms for the anti-inflammatory response?
Reduction in TNF-α production in LPS-challenged whole blood by Lyc-O-Mato drink supplementation

34% reduction

Riso, P, Visioli, F., Grande, S., Guarnieri, S., Gardana, C., Simonetti, P., and Porrini, M
A growing body of evidence demonstrates that these compounds can serve important functions independent of direct antioxidant chemistry, by modulating enzyme activity and gene expression.
What is the molecular mechanism of tomato carotenoids in skin protection from UV and oxidative damage?
Low and High Dose UVB Regulation of Transcription Factor NF-E2-Related Factor 2 (Nrf 2)

Sankaranarayanan Kannan and Anil K. Jaiswal

Department of Pharmacology, Baylor College of Medicine,

Cancer Res 2006; 66(17): 8421-9)
• They observed that low dose UVB exposure led to stimulation of Nrf 2 transcription factor and activation of chemo protective defense program.
• However, intriguingly, they found that high dose UVB exposure led to down-regulation of this protective mechanism.

• Suggesting that this contribute to environmental carcinogenic effects of UVB.
Carotenoids activate the antioxidant response element transcription system

Anat Ben-Dor, Michael Steiner, Larisa Gheber, Michael Danilenko, Noga Dubi, Karin Linnewiel, Anat Zick, Yoav Sharoni, and Joseph Levy

Department of Clinical Biochemistry, Faculty of Health Sciences, Ben-Gurion University of the Negev and Soroka Medical Center of Kupat Holim, Beer-Sheva 84105, Israel

Interestingly, part of the translocated Nrf2 colocalized with the promyelocytic leukemia protein in the promyelocytic leukemia nuclear bodies. The increase in phase II enzymes was abolished by a dominant-negative Nrf2, suggesting that carotenoid induction of these proteins depends on a functional Nrf2 and the ARE transcription system. [Mol Cancer Ther 2005;4(1):177–86]
Endogenous (dietary) Photoprotection by tomato oleoresin \textit{(Lyc-O-Mato)} is efficient as confirmed by Human intervention studies
Thank you
Antioxidants, positively affect skin texture

Dietary carotenoids provide moderate protection against UV-induced erythema (sunburn)

Carotenoids can be applied as supplements with the diet, or in enriched functional food products

For protection, doses > 10-15 mg carotenoids/day are needed; intervention > 6 wk

Antioxidant activity (and/or UV-absorption are) is the main mechanisms of protection