Effects of ingestion of tomatoes, tomato juice and tomato purée on contents of lycopene isomers, tocopherols and ascorbic acid in human plasma as well as on lycopene isomer pattern

Kati Fröhlich, Karin Kaufmann, Roland Bitsch and Volker Böhm*

Institute of Nutrition, Friedrich Schiller University Jena, Dornburger Strasse 25–29, D-07743 Jena, Germany

(Received 8 July 2005 – Revised 25 October 2005 – Accepted 25 October 2005)

Tomatoes are an important part of the diet. Lycopene, the predominant carotenoid in tomatoes, is hypothesised to mainly mediate the health benefits of tomato products. Anticancer activity of tomato products and lycopene has been suggested by numerous studies. The aim of the present study was to investigate the effect of ingestion of three different tomato-based foodstuffs on plasma contents of lycopene, tocopherols and ascorbic acid. Because isomers of lycopene may have different biological activities, a special interest was to look how the lycopene isomer pattern is changed depending on the matrix of tomato products. Following a 2-week depletion phase volunteers ingested 12.5 mg lycopene/d for 4 weeks comprising tomatos, tomato juice or tomato purée. The basal levels of lycopene in plasma were comparable for all groups and decreased significantly during the 2 weeks of depletion to approximately half of the basal values. Following intervention, plasma lycopene concentration increased significantly. Conversely, supplementation did not significantly affect levels of tocopherols and ascorbic acid in plasma. Regarding isomers of lycopene, the (Z)-lycopene/(all-E)-lycopene plasma isomer ratio was significantly changed during the study for all groups. A remarkable enrichment of the relative contents of (Z)-lycopene was observed during the depletion period, which supports the hypothesis that lycopene (Z)-isomers are formed within the human body after ingestion of (all-E)-lycopene. After dietary intervention with lycopene-rich products the isomer ratios returned to those observed at the start of the study. Further investigations will clarify the process of isomerisation in more detail.

Tomato products: (all-E)-Lycopene: Lycopene (Z)-isomers: Ascorbic acid: Tocopherols: Human bioavailability

Several epidemiological studies have indicated a beneficial effect of tomato consumption in the prevention of some major chronic diseases, such as some types of cancer (Giovannucci et al. 2002) and CVD (Klipstein-Grobusch et al. 2000). One of the major phytochemicals in tomato products contributing to the prevention of cancer is lycopene. Reports from epidemiological studies, studies in animals and cell-culture experiments have suggested that lycopene has anticancerogenic properties (Rao & Agarwal, 1999; Etminan et al. 2004; Tang et al. 2005). In addition to its antioxidant properties (DiMascio et al. 1989; Böhm et al. 2002), lycopene has also been shown to induce cell–cell communication (Zhang et al. 1991; Stahl et al. 2000), activate phase II enzymes (Breinholt et al. 2000), inhibit tumour cell proliferation (Levy et al. 1995), repress insulin-like growth factor receptor activation (Karas et al. 2000), and improve anti-tumour immune responses (Clinton, 1998). The mechanisms by which lycopene might exert its biological activities are still unknown.

The general structure of lycopene is an aliphatic hydrocarbon with eleven conjugated carbon–carbon double bounds, making it soluble in lipids and red in colour. Being acyclic, lycopene has no vitamin A activity. Recent investigations have shown that lycopene derivatives could activate retinoid receptors. However, the physiological significance has to be shown in future studies (Sharoni et al. 2004). Lycopene from tomatoes and tomato-based foods exists predominantly in the (all-E)-configuration, the thermodynamically most stable form (Porrini et al. 1998). In contrast, various (Z)-isomers account for over 50 % of blood lycopene and for over 75 % of tissue lycopene (Clinton et al. 1996; Ferruzzi et al. 2001). The processes that influence isomer patterns and the mechanisms of interconversion are still an essentially unexplored area of research. Isomerisation of lycopene may have significant consequences since the large three-dimensional differences between these geometric isomers may influence their pharmacological properties (Holloway et al. 2000). Recent investigations using the Trolox equivalent antioxidant capacity assay have shown significantly different antioxidant activity for lycopene isomers depending on the geometrical structure (Böhm et al. 2002).

The aim of the present study was to explore the interrelationships among the intake of different commonly consumed tomato products (tomatoes, tomato juice, tomato purée), plasma lycopene isomer profiles and plasma levels of ascorbic acid and tocopherols. All volunteers were supplied with a daily dosage of 12.5 mg lycopene for 4 weeks after a 2-week diet low in lycopene.

Subjects and methods

Subjects and study design

Seventeen subjects (fourteen women and three men) ranging from 19 to 25 years with a BMI between 19 and 25 kg/m²

* Corresponding author: Dr Volker Böhm, fax +49 3641 949632, email Volker.Boehm@uni-jena.de

Downloaded from https://www.cambridge.org/core. IP address: 54.191.40.80, on 07 Apr 2017 at 12:37:15, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms. https://doi.org/10.1079/BJN20051657
participated in the study. They were divided randomly into three groups (tomato group, tomato juice group, tomato purée group). Characteristics of the subjects are summarised in Table 1. The participants were non-smokers and did not take carotenoid supplements or vitamin A supplements. Informed written consent was obtained from each participant and the protocol was approved (ethical vote no. 0913-07/02) by the Ethical Committee of the Friedrich Schiller University Jena at the Medical Faculty (Bachstrasse 18, 07743 Jena, Germany). Subjects were asked to follow precise instructions regarding their diet to limit carotenoid intake without interfering with their own eating habits. All subjects avoided food rich in lycopene such as tomatoes and tomato products, watermelons, yellow and red peppers, pink grapefruit, papayas, apricots, guavas, rosehip products and sea-buckthorn products for a 2-week depletion period and the following 4 weeks of intervention. After the depletion period, they ingested 12·5 mg lycopene/d with breakfast for 4 weeks, either from 145–320 g tomatoes/d, 94–101 g tomato juice/d or 25–28 g tomato purée/d. They were asked to consume tomatoes and tomato products with a small portion of dietary fat (exact amount was not determined) to guarantee the absorption of lycopene. All intervention products (different batches were only available due to the large amounts needed) were purchased in a local store. The lycopene content of the tomato products was analysed before the start of the study, the lycopene content of the tomatoes after each purchase, in order to calculate the equivalent amounts for the participants. Detailed compositions of the tomato products are shown in Table 1.

Collection of blood samples

Fasting blood samples (10 ml) were withdrawn from the study participants in EDTA tubes before the study (T–2), after the 2 weeks of depletion (T0) and thereafter weekly while participants in EDTA tubes before the study (T–2), after the 2 weeks of depletion (T0) and thereafter weekly while the 2 groups (tomato group, tomato juice group, tomato purée group). Characteristics of the subjects are summarised in Table 1. The participants were non-smokers and did not take carotenoid supplements or vitamin A supplements. Informed written consent was obtained from each participant and the protocol was approved (ethical vote no. 0913-07/02) by the Ethical Committee of the Friedrich Schiller University Jena at the Medical Faculty (Bachstrasse 18, 07743 Jena, Germany). Subjects were asked to follow precise instructions regarding their diet to limit carotenoid intake without interfering with their own eating habits. All subjects avoided food rich in lycopene such as tomatoes and tomato products, watermelons, yellow and red peppers, pink grapefruit, papayas, apricots, guavas, rosehip products and sea-buckthorn products for a 2-week depletion period and the following 4 weeks of intervention. After the depletion period, they ingested 12·5 mg lycopene/d with breakfast for 4 weeks, either from 145–320 g tomatoes/d, 94–101 g tomato juice/d or 25–28 g tomato purée/d. They were asked to consume tomatoes and tomato products with a small portion of dietary fat (exact amount was not determined) to guarantee the absorption of lycopene. All intervention products (different batches were only available due to the large amounts needed) were purchased in a local store. The lycopene content of the tomato products was analysed before the start of the study, the lycopene content of the tomatoes after each purchase, in order to calculate the equivalent amounts for the participants. Detailed compositions of the tomato products are shown in Table 1.

Table 1. The main characteristics of the subjects participating in the study and composition of the supplemented tomato products (Mean values and standard deviations)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Tomato</th>
<th>Tomato juice</th>
<th>Tomato purée</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (years)</td>
<td>Mean 6</td>
<td>Mean 6</td>
<td>Mean 5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>23.0 0.6</td>
<td>22.8 2.2</td>
<td>22.4 1.7</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>61.7 5.4</td>
<td>62.8 8.7</td>
<td>60.7 6.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.7 1.7</td>
<td>21.4 1.8</td>
<td>20.4 1.9</td>
</tr>
<tr>
<td>Tomato products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total-lycopene (mg/100g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>3.9 0.3</td>
<td>11.5 0.6</td>
<td>44.4 1.9</td>
</tr>
<tr>
<td>Maximum</td>
<td>8.7 0.4</td>
<td>12.4 0.7</td>
<td>50.5 3.4</td>
</tr>
<tr>
<td>Ascorbic acid (mg/100g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>4.0 0.1</td>
<td>5.8 0.2</td>
<td>34.5 0.7</td>
</tr>
<tr>
<td>Maximum</td>
<td>7.2 0.1</td>
<td>6.7 0.3</td>
<td>35.4 0.6</td>
</tr>
<tr>
<td>Total tocopherol (μmol/100g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>0.34 0.01</td>
<td>2.75 0.06</td>
<td>11.82 0.90</td>
</tr>
<tr>
<td>Maximum</td>
<td>0.66 0.01</td>
<td>2.87 0.01</td>
<td>15.23 0.35</td>
</tr>
</tbody>
</table>

For details of subjects and procedures, see p. 734.

Analysis of carotenoids

Carotenoids were extracted according to Bieri et al. (1985), slightly modified. An equal volume of ethanolic echinone (kind gift of DSM Nutritional Products, Basel, Switzerland) solution (internal standard) was added to 500 μl plasma. The sample was mixed using a vortex for 30 s before addition of 250 μl hexane with 0·1 % butylated hydroxytoluene. The mixture was shaken for 1 min and centrifuged at 14 000 rpm for 2 min. The plasma extraction procedure was performed three times on each sample to ensure total removal of carotenoids. The combined hexane layers were evaporated to dryness using a gentle stream of N₂ at 30 ± 1°C. The residue was dissolved in 250 μl methanol–methyl tert-butylether (1:1, v/v), vortexed and centrifuged at 14 000 rpm for 4 min. The supernatant fraction was analysed on a C18, (250 × 4.6 mm, 5 μm) column (YMC Europe, Schermbeck, Germany), preceded by a C18 ProntoSil 120-5-C18 (10 × 4.0 mm, 5 μm) column (Bischoff, Leonberg, Germany) at 23 ± 1°C with diode array detection at 450 nm (Böhm, 2001). As mobile phase (1:3 ml/min) the following gradient procedure was used consisting of methanol (solvent A) and methyl tert-butyl ether (solvent B): (1) initial conditions 90 % solvent A and 10 % solvent B; (2) a 55 min linear gradient to 55 % solvent B; (3) 45 % solvent A and 55 % solvent B for 5 min; (4) a 10 min linear gradient to 10 % solvent B. All experiments were carried out under subdued light to prevent photodegradation and isomerisation. Recovery (n 280) of the internal standard was 96 ± 12 %. (all-E)-Lycopene was identified using reference material, which was a kind gift of DSM Natural Products. (all-E)-Lycopene stock solution in cyclohexane–toluene (4:1, v/v) of 83 μg/ml was prepared and diluted daily 1:100 using a mixture of methanol and methyl tert-butyl ether (1:1, v/v) to obtain the working solution. The concentration of the stock solution was checked periodically by using its extinction coefficient (E (1 %, 1 cm): 3450 (n-hexane, 472 nm) (Craft et al. 2000)). The lycopene (Z)-isomers were quantified by using the (all-E)-lycopene calibration. Different spectroscopic techniques were used to identify the main lycopene (Z)-isomers (Fröhlich et al. 2005).

Tomato products were analysed on their carotenoid contents as recently described elsewhere (Seybold et al. 2004).

Analysis of ascorbic acid

The content of ascorbic acid was determined by using a spectrophotometrical method according to Speitling et al. (1992). TCA (300 μl) was mixed with 200 μl of standard solutions (calibration straight line), plasma (which had been already prepared before storage at −80°C) or distilled water (blank reading value). The reaction mixture was vortexed and centrifuged (12 000 rpm; 5 min). Samples of 300 μl of the supernatant fraction were mixed with 100 μl dinitrophenylhydrazine-reagent (2 g/100 ml). The mixture was vortexed again, incubated at 60°C on a thermal shaker for 1 h and cooled on ice for 5 min. Then 400 μl sulfuric acid were added to the reaction mixture. After vortexing and keeping in the dark for 20 min, the mixture was immediately stabilised with TCA. All plasma samples were stored at −80°C until analysis. Blood samples and plasma samples were always handled under subdued light.
was vortexed once again before spectrophotometrical analysis at 520 nm against the blank reading. Tomatoes, tomato juice and tomato purée were analysed on their contents of ascorbic acid as recently described elsewhere (Gahler et al. 2003) by using the spectrophotometrical determination as mentioned earlier for the plasma samples instead of the HPLC determination described there.

**Analysis of tocopherols**

Plasma (500 μl) was extracted by adding 400 μl ethanol containing 0.1 % BHT. The mixture was vortexed for 30 s. After the addition of 400 μl n-hexane the mixture was vortexed again for 1 min and centrifuged at 14 000 rpm for 4 min. The extraction was repeated three times and the combined organic phases were evaporated to dryness under N₂ at 30 ± 1°C. The residue was dissolved in 1 ml of mobile phase, vortexed and centrifuged (14 000 rpm, 4 min). The supernatant fraction was analysed on a diol-column by using n-hexane–methyl tert-butyl ether (96:4, v/v) as mobile phase at a column temperature of 50°C with fluorescence detection (Balz et al. 1992). Plasma tocopherol concentration was calculated by means of peak areas of the respective standards: α-, β-, γ-, δ-tocopherols (Calbiochem, Darmstadt, Germany).

Tomato products were analysed on their tocopherol contents as recently described elsewhere (Seybold et al. 2004) by using the same HPLC method as mentioned earlier for the plasma samples.

**Statistical analysis**

Results are expressed as means and standard deviations. Differences between variables were tested for significance by using the one-way ANOVA procedure (Tukey) for the basal values and for all other results the general linear model for the two-way ANOVA procedure (SPSS for Windows, release 10.07 (June 2000; SPSS Inc., Chicago, IL, USA)), using a level of significance of P < 0.05. Results were defined as ‘comparable’ if P > 0.05.

**Results**

A representative HPLC chromatogram demonstrating plasma separation of lycopene isomers in human plasma is shown in Fig. 1. Results were calculated as total lycopene, including (all-E)-, (13Z)-, (5Z,9’Z)-, (9Z)-, (5Z,9Z)- and (5Z)-lycopene as well as any not yet identified (Z)-isomer of lycopene and the contents of the isomers separately. The contents of several isomers of lycopene are shown in Fig. 2. The lycopene concentrations of tomatoes, tomato juice and tomato purée used in the present study are presented in Table 1. (all-E)-Lycopene is the predominant isomer in each tomato product, accounting for 90–95 % of total lycopene in tomatoes, 95–98 % in tomato juice and 92–94 % in tomato purée.

**Total lycopene**

Total lycopene plasma levels of the three groups of volunteers are shown in Fig. 3. Basal mean lycopene levels of all groups were in a comparable range (P > 0.05) between 0.57 and 0.78 μmol/l. After the 2-week diet with low lycopene intake, the total plasma lycopene concentration decreased (P < 0.05) to 45–62 % of the basal values. The total lycopene plasma levels were significantly enhanced (P < 0.05) relative to the depleted state from 0.25 (sd 0.14) to 0.39 (sd 0.23) μmol/l after 1 week of supplementation with tomatoes. Tomato juice also led to significantly (P < 0.05) increased lycopene plasma levels after 1 week of supplementation from 0.43 (sd 0.15) to 0.61 (sd 0.17) μmol/l. The total lycopene plasma levels remained nearly stable during the next 3 weeks of supplementation. Supplementation with tomato purée led to significantly enhanced (P < 0.05) plasma levels of lycopene after 2 weeks of intervention (0.37 (sd 0.19) to 0.74 (sd 0.24) μmol/l). After 4 weeks of intervention with tomato products the increase of total lycopene in plasma was comparable (P > 0.05) for the three food matrices investigated. The total lycopene plasma levels at T4 of all groups (0.53–0.81 μmol/l) were not significantly different (P > 0.05) from the basal levels (T-2).

**Isomers of lycopene**

The plasma levels of the several isomers of lycopene are shown in Fig. 2. The two major lycopene isomers in plasma of all volunteers were (all-E)- and (5Z)-lycopene. Decreases and increases in contents of both (Z)- and (all-E)-isomers of lycopene led to changes in concentrations of total lycopene within all intervention trials. Looking at alterations of the concentrations of the different (Z)-isomers of lycopene, only the (13Z)-lycopene showed significantly lower concentrations in plasma after intervention with tomatoes compared with tomato juice and tomato purée. The other lycopene isomers did not show significant (P > 0.05) differences among the three groups. The ratios of the sum of all evaluated lycopene (Z)-isomers: (all-E)-lycopene were used for assessment of isomer changes in plasma. The (Z)-lycopene: (all-E)-lycopene isomer ratio was reversed during the study for all groups. The percentages of diverse lycopene isomers are shown in Table 2. Plasma isomer concentration showed an approximately 60:40 ratio of (Z)/(all-E) at the start of the study. After a 2-week depletion period during which the participants consumed a diet low in lycopene, the ratios had changed. A decrease in the (all-E)-configuration to approximately 30 % of total lycopene and a compensatory increase of the (Z)-isomers to 70 % was observed. After 4 weeks of dietary intervention with tomato juice (63 % (Z); 37 % (all-E)) and tomato purée (61 % (Z); 39 % (all-E)) isomer ratios returned to those of the predominant isomer (5Z)-lycopene.
observed at the start of the study. After 4 weeks of intervention with raw tomatoes the (Z):(all-E) ratio was 50:50.

Ascorbic acid and tocopherols

The contents of the antioxidant vitamins ascorbic acid and tocopherols in plasma did not change significantly (P > 0.05) during the depletion period and were not affected by 4 weeks of supplementation with tomatoes or tomato products (data not shown).

Discussion

In the present study, volunteers ingested 12.5 mg lycopene/d from tomatoes, tomato juice and tomato purée. This is approximately a tenfold higher dose than those described in the German National Food Consumption Survey (Pelz et al. 1998). This high lycopene amount was chosen to guarantee sufficient detection of minor compounds in plasma such as some (Z)-lycopene isomers. Furthermore, 145–320 g tomatoes, 94–101 g tomato juice and 25–28 g tomato purée daily are in accordance with consumable amounts of tomato products.

At the end of a 2-week depletion period with a diet low in lycopene, the total plasma lycopene concentration decreased significantly (P < 0.05) to 53 % (range 45–62 %) of the basal values. Other publications have reported comparable plasma lycopene clearance rates (Böh m & Bitsch, 1999; Allen et al. 2003).

The daily consumption of commercially available tomatoes and tomato products rapidly and significantly increases blood lycopene concentrations. The present study showed
Tomatoes

Table 2. Relative contents of lycopene isomers over time in subjects consuming daily portions of tomatoes or tomato products for 4 weeks after a 2-week depletion period. Values are means, with standard deviations represented by vertical bars. For details of subjects and procedures, see p. 734.

<table>
<thead>
<tr>
<th></th>
<th>T–2 (%)</th>
<th>T0 (%)</th>
<th>T1 (%)</th>
<th>T2 (%)</th>
<th>T3 (%)</th>
<th>T4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tomato juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(all-E)</td>
<td>39·5</td>
<td>4·1</td>
<td>30·3</td>
<td>4·5</td>
<td>45·4</td>
<td>4·7</td>
</tr>
<tr>
<td>(1Z)</td>
<td>7·3</td>
<td>4·0</td>
<td>11·9</td>
<td>5·5</td>
<td>9·1</td>
<td>3·9</td>
</tr>
<tr>
<td>(Z), unidentified</td>
<td>9·0</td>
<td>2·7</td>
<td>10·1</td>
<td>2·2</td>
<td>13·1</td>
<td>2·0</td>
</tr>
<tr>
<td>(5Z,9Z) + (9Z) + (5Z,9Z)</td>
<td>10·0</td>
<td>2·4</td>
<td>11·7</td>
<td>3·2</td>
<td>8·7</td>
<td>1·4</td>
</tr>
<tr>
<td>(5Z)</td>
<td>34·2</td>
<td>4·5</td>
<td>36·0</td>
<td>6·5</td>
<td>23·7</td>
<td>3·6</td>
</tr>
<tr>
<td>Tomato puree</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(all-E)</td>
<td>39·2</td>
<td>4·6</td>
<td>30·5</td>
<td>5·6</td>
<td>34·1</td>
<td>5·1</td>
</tr>
<tr>
<td>(1Z)</td>
<td>20·7</td>
<td>3·4</td>
<td>22·3</td>
<td>5·3</td>
<td>23·5</td>
<td>3·5</td>
</tr>
<tr>
<td>(Z), unidentified</td>
<td>6·5</td>
<td>2·4</td>
<td>7·6</td>
<td>3·5</td>
<td>8·9</td>
<td>3·0</td>
</tr>
<tr>
<td>(5Z,9Z) + (9Z) + (5Z,9Z)</td>
<td>6·2</td>
<td>2·9</td>
<td>7·5</td>
<td>2·8</td>
<td>7·2</td>
<td>2·7</td>
</tr>
<tr>
<td>(5Z)</td>
<td>27·5</td>
<td>3·8</td>
<td>32·1</td>
<td>2·9</td>
<td>26·3</td>
<td>2·3</td>
</tr>
</tbody>
</table>

For details of subjects and procedures, see p. 734.
Lycopene isomers after human intervention

isomers at baseline, a finding consistent with other reports (Clinton et al. 1996; Schierle et al. 1997; Holloway et al. 2000; Richelle et al. 2002). During the depletion period, a significant change in the (Z):(all-E) isomeric ratios from approximately 60 % (Z), 40 % (all-E) before the study to 70 % (Z), 30 % (all-E) after 2 weeks on a lycopene-free diet was observed. Comparable changes in the (Z):(all-E) ratios of lycopene in human plasma were described in another study. Hadley et al. (2003) showed a significant decrease of (all-
E)-lycopene as a percentage of plasma total lycopene isomers from 44.4 (SEM 1.2) % to 39.6 (SEM 1.2) %, whereas total (Z)-isomers increased from 55.6 (SEM 1.2) % to 60.4 (SEM 1.2) % during a 1-week washout period. The percentage of (all-E)-lycopene also decreased after 3 weeks on a lycopene-free diet in a study by Edwards et al. (2003). Conversely, a study by Müllert et al. (1999) did not find a significant difference in the (Z):(all-E)-lycopene ratio during a 2-week washout period. This decrease in the relative proportion of (E)-lyco-
pene of total lycopene in plasma may be a result of several simultaneous processes, including a more rapid clearance of (all-E)-lycopene, a greater tissue uptake of (all-E)-lycopene or conversion to (Z)-isomers in the human body. In addition, the possible mobilisation of lycopene from tissue stores where lycopene is predominantly found in the cis form may contribute to a relative increase in the plasma (Z)-isomer pool.

After 4 weeks of intervention with tomato juice and tomato purée (with the exception of tomatoes) the (Z):(all-E)-lyco-
pene ratio returned to those observed at the beginning of the study. Other studies confirmed these findings. Holloway et al. (2000) reported that (all-E)-lycopene increased to 40–45 % of plasma lycopene after 2 weeks of supplementation with 21 mg lycopene/d comprising tomato paste. Similarly, the percentage of (all-E)-lycopene increased significantly from 30–32 at baseline to 44–46 after 3 weeks of intervention with waterme-
on juice (Edwards et al. 2003). However, Hadley et al. (2003) observed a decrease of the relative contents of (5Z)-lycopene in a study where sixty volunteers ingested 23–55 mg lyco-
pene/d comprising tomato products for 15 d. The observations suggest that maintaining a stable (all-E):(Z) isomers ratio in the blood requires continued dietary intake of the (all-E) form being predominant in food. It is also possible that lyco-
pene exists in plasma as a mixture of (all-E) and (Z)-isomers of lycopene because this mixture is the thermodynamically most stable equilibrium of different geometric isomers.

Accumulating evidence in human subjects (Stahl & Sies, 1992; Gärntner et al. 1997; Boileau et al. 2002) and in animal models (Boileau et al. 1999) supports the hypothesis that (Z)-lycopene isomers are preferentially absorbed to (E)-lycopene. This may be the result of a greater solubility of (Z)-isomers in mixed micelles and a lower tendency to aggre-
gate (Britton, 1995). A study from Re et al. (2001) reported that a high percentage of (Z)-lycopene isomers is present in tissues because it is better absorbed than (E)-lycopene from the gastrointestinal tract. Therefore, the increase in plasma concentrations of (Z)-isomers following administration of pro-
ducts containing lycopene is not solely related to the content of dosed (Z)-lycopene isomers. The elevated content of differ-
ent (Z)-isomers in plasma may account for a longer residence time, which is in line with a longer half-life for (Z)-isomers compared with that of (all-E)-lycopene (Cohn et al. 2002). Alternative explanations are isomerisation of systemic available (all-E)-lycopene within the human body. Isomerisa-
tion of (all-E)-lycopene to (Z)-lycopene is likely to occur during digestion (Re et al. 2001), but only after (all-E)-lyco-
pene is released from the food matrix, in which it is fairly stable (Nguen & Schwartz, 1998). The presence of acid in the stomach is perhaps the most plausible cause of (Z)-isomer formation, but this does not explain the diversity in the distribution of geometrical carotenoid isomers found in different organs of the body. A recent human intervention study showed that there was no significant (E)→(Z) isomerisa-
tion of lycopene in the human stomach. The fact that lycopene (Z)-isomers are poorly transported by the chylomicrons and thus poorly absorbed strongly suggested that a (E)→(Z) iso-
erisation of lycopene occurs in the human body at a post-
enterocyte level (Tyssandier et al. 2003). Future investigations are necessary to assess whether: (1) (Z)-lycopene isomers are preferentially absorbed in human subjects; (2) (all-E)-lyco-
pene is converted into (Z)-isomers after absorption; (3) (Z)-

isomers of lycopene mobilised from body stores to plasma or (all-E)-lycopene is preferentially degraded in the plasma compared with (Z)-lycopene. It is supposed that a combination of several mechanisms occurs in the human body.

Regarding vitamin C and E, no significant differences were observed in the plasma contents of ascorbic acid and tocopher-
ols (P>0.05) during the entire study period, although both vitamins were ingested with the tomatoes and tomato pro-
ducts. Tyssandier et al. (2004) also did not detect any change in plasma ascorbic acid and tocopherols in a study in which subjects ingested 96 g tomato purée/d for 3 weeks. The plasma concentrations of these micronutrients are mainly correlated with the dietary intake of these compounds, with tomatoes and tomato products contributing a minor part.

In conclusion, ingestion of 12.5 mg lycopene/d for 4 weeks as tomatoes, tomato juice and tomato purée resulted in signific-
antly increased plasma concentration of total lycopene. Under the conditions in the present study, lycopene appeared to be approximately equally bioavailable from the three com-
modities. Looking at alterations of the relative contents of the lycopene isomers, the (Z):(all-E)-lycopene isomer ratio was reversed during the study for all groups. A remarkable enrich-
m ent of the relative contents of (Z)-lycopene was observed during the depletion period. After dietary intervention with lycopene-rich products the isomer ratio regained a state compara-
ble with those observed at the beginning of the washout period. Further investigations will clarify the process of iso-
erisation of lycopene in more detail.

Acknowledgements

DSM Nutritional Products, Basel, Switzerland, is gratefully acknowledged for supplying the carotenoid reference materials. The authors are indebted to H. Schmidt and I. Schmuck for their technical assistance and to T. Franke for withdrawal of blood. Finally, thanks are also given to all study participants.

References


Stahl W & Sies H (1992) Uptake of lycopene and its geometrical iso-
mers is greater from heat-processed than from unprocessed tomato 

Stimulation of gap junctional communication: comparison of 
acetyl-retinoic acid and lycopene. *Arch Biochem Biophys* **373**, 
271–274.

growth of human androgen-independent prostate cancer cells in 

of tomato product consumption on the plasma status of antioxidant 
microconstituents and on the plasma total antioxidant capacity in 

Tyssandier V, Reboul E, Dumas J-F, Bouteloup-Demange C, Armand 
borne carotenoids in the human stomach and duodenum. *Am J Phys-

van het Hof KH, de Boer BC, Tijburg LB, Lucius BR, Zijp I, West 
CE, Hautvast JG & Weststrate JA (2000) Carotenoid bioavailabil-
ity in humans from tomatoes processed in different ways deter-
mined from the carotenoid response in the triglyceride-rich-
lipoprotein fraction of plasma after a single consumption and in 

Zhang L-X, Cooney RV & Bertram JS (1991) Carotenoids enhance 
gap junctional communication and inhibit lipid peroxidation in 
C3H/10T1/2 cells: relationship to their cancer chemopreventive 