Short Communication

Vegetable oil-mediated thermal isomerization of \((all-E)\)-lycopene: Facile and efficient production of Z-isomers

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Thermal isomerization of \((all-E)\)-lycopene to the corresponding Z-isomers was investigated in edible vegetable oils; perilla, linseed, grape seed, soybean, corn, sesame, rapeseed, rice bran, safflower seed, olive, and sunflower seed oil. Purified \((all-E)\)-lycopene from tomato oleoresin was converted to Z-isomers in the range of 44.8–58.8% content, and the remaining ratio of total amount of lycopene isomers without decomposition were ranged from 38.8 to 79.6% after heating at 100°C for 1 h in the vegetable oils. Both values were exceedingly high in sesame oil: 58.8% of total Z-isomers content and 78.3% of remaining lycopene. In particular, \((5Z)\)-lycopene, which has higher bioavailability and antioxidant capacity as well as greater storage stability among the Z-isomers, was notably increased in that oil; approximately threefold higher than the average of the other vegetable oils.

Practical applications: Lycopene offers many health benefits such as decreased risk of cancer and arteriosclerosis. The Z-isomers of lycopene, occurring in processed tomato products, are more bioavailable than the \(all-E\)-isomer which is a major configuration form in raw tomatoes. This study has developed an efficient production method for Z-isomers of lycopene by heating \((all-E)\)-lycopene in edible vegetable oils, in which neither organic solvents nor food additives are used. It would be practically feasible to utilize this procedure for the food, drink, and dietary supplement manufacturing, as well as for daily cooking at home.

Keywords: Carotenoids / Lycopene / Sesame oil / Thermal isomerization / Vegetable oils

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1 Introduction

Lycopene is one of the most widespread and representative carotenoids, especially rich in vegetables and fruits such as tomatoes, gac, and watermelon [1, 2]. Several studies have indicated that the adequate ingestion of lycopene can significantly lower the risk of cancer and arteriosclerosis [3, 4]. While lycopene in fresh tomato fruits is accumulated predominantly as the \((all-E)\)-configuration, the Z-isomers of lycopene such as \((5Z)\)-, \((9Z)\)-, and \((13Z)\)-lycopene are primarily found in the human body (Supporting Information Fig. S1). For example, in sera and cellular tissues of humans more than half of total lycopene was identified as the Z-forms [5, 6]. Interestingly, the observations from in vitro and in vivo experiments using cultured small intestinal cells [7] and ferrets [8], respectively, have demonstrated a greater potential for bioavailability of the Z-isomers. In fact, lycopene concentrations in human plasma substantially increased by the ingestion of tomato sauce rich in Z-isomers of lycopene compared with a sample abundant in the \(all-E\)-isomer [9]. Moreover, it has been reported that certain Z-isomers, such as \((5Z)\)-lycopene and \((7Z,9Z,7'Z,9'Z)\)-lycopene (prolycopene), have higher antioxidant capacities than \(all-E\)-isomer [10]. For these reasons, the intake of Z-isomers of lycopene, rather than \(all-E\)-isomer, is preferable for human health, and appropriate methods are required to enable the efficient Z-isomerization of \((all-E)\)-lycopene.
Recently, we reported basic studies on the thermal- and photo-isomerization of \((all-E)\)-lycopene, and finally attained a greater isomerization to the corresponding \(Z\)-isomers (79.9% conversion) in the presence of a catalyst [13] almost without degradation of lycopene (96.5% recovery). Although our developed methods showed high efficiency for geometrical isomerization of \((all-E)\)-lycopene and are amenable to foods and beverages manufacturing, some organic solvents or food additives such as erythrosine and iron(III) chloride were employed in each procedure. Since the global trend is toward natural and additive-free foods and drinks, we embarked on a new study on lycopene preparations rich in \(Z\)-forms without those chemical reagents.

Several studies have also reported that some organic solvents, such as dichloromethane and chloroform, promoted thermal \(Z\)-isomerization of carotenoids including lycopene [14–16], and have stimulated interest in the possible effects induced by biogenic solvents like vegetable oils. Here, we investigated the potential of \(I\) different kinds of edible vegetable oils available in the market to isomerize \((all-E)\)-lycopene to \(Z\)-isomers under heat treatment. This simple but effective method will be an alternative tool for the \(Z\)-isomerization of \((all-E)\)-lycopene under conditions suitable for food processing.

2 Materials and methods

2.1 Materials

All solvents were of analytical-grade, except for the HPLC-grade methanol (Sigma-Aldrich, St. Louis, MO) and vegetable oils for cooking (perilla, linseed, grape seed, soybean, corn, sesame, rapeseed, rice bran, safflower seed, olive, and sunflower seed oils). The suppliers of the oils are summarized in Supporting Information Table S1 with some chemical properties [17–20].

2.2 Purification of \((all-E)\)-lycopene

\((all-E)\)-Lycopene was obtained from tomato oleoresin (Lyc-O-Mato° 15%, LycoRed Ltd., Beer-Sheva, Israel) according to the previous description [11]: 493.4 mg of fine red crystalline powder from 3.12 g of tomato material; reversed-phase HPLC, ≥98.3% purity. Purified lycopene was stored at \(-80^\circ\)C until just before use.

2.3 Thermal isomerization of purified \((all-E)\)-lycopene in vegetable oils

The edible vegetable oils used in this study were perilla, linseed, grape seed, soybean, corn, sesame, rapeseed, rice bran, safflower seed, olive, and sunflower seed oil. Purified \((all-E)\)-lycopene was dispersed into each vegetable oil at the concentration of 10 mg/mL, and the residues were dissolved by sonication in an ice-cold bath (SUS-300, Shimadzu, Kyoto, Japan) at 300 W for 20 min. Almost no isomerization of \((all-E)\)-lycopene was observed after the process: 99.7 ± 0.9% of the initial \((all-E)\)-lycopene remained as it was. From each of the solutions, 25 \(\mu\)L of sample was withdrawn with a microsyringe, transferred to a small vial, and the headspace was purged with argon gas. Immediately, the vessels were tightly closed to minimize the oxygen exposure and placed in an oil-bath under dark conditions. Isomerization was conducted at 100°C for 1 or 3 h based on previous studies [21, 22]. After the thermal treatment, each reaction mixture was diluted in 5 mL of benzene and filtered through a 0.2\(\mu m\) polytetrafluoroethylene membrane filter (Advantec Co., Ltd., Tokyo, Japan) prior to the HPLC separation.

2.4 HPLC analysis

Reversed-phase HPLC analysis with a \(C_{30}\) carotenoid column \((250 \times 4.6\ mm\ i.d.,\ 5 \mu m,\ YMC,\ Kyoto)\) was conducted according to the method described previously [11]. The quantification of \(Z\)-isomers of lycopene was carried out by peak area integration at 470 nm by a UV-vis detector (JASCO Co., Tokyo), and the peaks were identified by retention time and UV spectra, absorption maxima \((\lambda_{\text{max}})\) and relative intensities of the \(Z\)-peak \((% D_9/D_0)\), referring to previous works [5, 11–14].

3 Results and discussion

Purified \((all-E)\)-lycopene samples dissolved in corn and sesame oils, which are nearly equivalent in iodine values (IV) and saponification values (SV) and fatty acid (FA) compositions (Supporting Information Table S1) [19, 20], were thermally isomerized at 100°C for 1 h. The resulting lycopene mixtures were separated on a reversed-phase HPLC column. The typical chromatogram of each sample is shown in Fig. 1, as well as that of intact \((all-E)\)-lycopene. The predominant mono-\(Z\)-isomers produced were identified according to previous works [11–14] and defined spectral data for \((5Z)\)-lycopene (Supporting Information Tables S2 and S3). In corn oil (Fig. 1B), (9\(Z\))- and (13\(Z\))-lycopene were prevailing except for the \(all-E\)-form, while \((5Z)\)-lycopene and putative \((5Z,9Z)\)– and \((5Z,9Z)\)-isomers [23] were significantly increased in sesame oil (Fig. 1C). These mono-\(Z\)-isomers are often found in the human body as well as in processed tomato products [5, 6]. Some peaks assumed (multi-\(Z\))-lycopene were also detected in both vegetable oils.

Thermal isomerization of \((all-E)\)-lycopene to the \(Z\)-isomers was conducted in various kinds of vegetable oils having different IV at 100°C for 1 h. The percentage contents of the isomers obtained are listed in Table 1. The total content of \(Z\)-lycopene surpassed 58.8% after the heat
treatment in sesame oil, and the values attained in the 11 vegetable oils were higher in the order corresponding to sesame > rice bran, grape seed, safflower seed, soybean, corn, linseed > olive, rapeseed, perilla > sunflower seed oil. As for the individual Z-isomers generated, profiles of components of the Z-isomers were almost the same among the tested vegetable oils except for sesame oil, in which (5Z)-lycopene increased approximately 3–5 times compared with the others. (5Z)-Lycopene was estimated to be kinetically unfavorable but thermodynamically more stable than (9Z)- and (13Z)-lycopene by the results of quantum chemistry calculations [25, 26]. The preferential occurrence of (5Z)-lycopene from (all-E)-lycopene in sesame oil is considered to be independent of the IV and SV and FA composition, because these values were similar to those of corn oil [19, 20]. Colle et al. [27] also indicated that there was no correlation between these values and thermal isomerization tendencies of (all-E)-lycopene by the experiments of using olive and fish oils. It can be supposed that the preference is due to the catalytic ingredients in sesame oil, such as iron, which increased a content of (5Z)-isomer [13] maybe by lowering the activation energy during isomerization to the corresponding isomer [25, 26]. Interestingly, (5Z)-lycopene has been reported to show higher bioavailability [28] and antioxidant capacity [10] compared with (all-E)-lycopene and possibly to (9Z)- and (13Z)-lycopene.

The remaining ratios of total amount of lycopene isomers without decomposition were investigated under the above conditions, and found to be high in the following order: sunflower seed, sesame, soybean, rapeseed, corn, olive, safflower seed, rice bran (79.6–72.4%) > perilla, grape seed (55.8, and 54.1%, respectively) > linseed oil (38.8%) (Supporting Information Table S4). The decomposition of lycopene in oils showing higher remaining ratios, such as sunflower seed and sesame oils, would probably be suppressed by natural antioxidants contained in the oils, such as α-tocopherol and sesamol, respectively [20]. In fact, proton nuclear magnetic resonance signals at 5.95 and 6.77–6.88 ppm, possibly derived from the spectra of lignan derivatives [29], were observed in a sesame oil used in this study. On the other hand, lycopene was largely degraded in perilla, linseed, and grape seed oil. The high IV of these oils brought about the accelerated degradation of lycopene, because the double bonds in FA can undergo the formation of peroxy radicals harmful to lycopene [20, 27].

As a practically important criterion, efficiency of Z-isomerization with vegetable oils was assessed for the Z-isomers of lycopene in total amount and for 5Z-isomer, considering the remaining ratio of total amount of lycopene isomers without decomposition after the thermal treatment (Fig. 2). In eight oils, more than 35% of the efficiency of total Z-isomerization could be attained for 1 h, whereas only two oils showed such high efficiency after 3 h (Fig. 2A). When sesame oil was employed, the efficiency remained above 45% during the period tested, and in particular, (5Z)-lycopene production was threefold greater than the average of the other oils (Fig. 2B). The thermal Z-isomerization efficiency of (all-E)-lycopene in sesame oil is estimated to be higher than in common organic solvents such as acetone, benzene, and hexane: approximately 40% of total Z-isomers content and less than 3% of (5Z)-lycopene content by heating in those solvents, even without considering the decomposition of lycopene [14]. In perilla and linseed oils, however, the efficiencies were quite low at ca. 5% for total Z-isomers and less than 0.5% for (5Z)-lycopene for 3 h, because high
decomposition ratios of lycopene depend on the high IV discussed above. In this study, we found that \((\text{all-}E)\)-lycopene was efficiently isomerized to \(Z\)-isomers by heating in sesame oil. The \(Z\)-isomers of lycopene, however, might be easily decomposed by oxidation than \(\text{all-}E\)-form done [30]. Thus, further investigations are in progress to improve the storage stability of the \(Z\)-isomers.

### 4 Conclusions

The thermal isomerization of \((\text{all-}E)\)-lycopene in edible vegetable oils was investigated for individual \(Z\)-isomers of lycopene quantitatively, and has demonstrated to be highly effective to obtain the isomers with ease for food processing. Especially in sesame oil, \((5Z)\)-lycopene, which has higher

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**Table 1.** Isomerization of \((\text{all-}E)\)-lycopene to \(Z\)-isomers in various vegetable oils by heating at 100°C for 1 h

<table>
<thead>
<tr>
<th>Vegetable oil</th>
<th>((\text{all-}E))</th>
<th>Total ((Z))</th>
<th>((5Z))</th>
<th>((9Z))</th>
<th>((13Z))</th>
<th>Other ((Z))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perilla</td>
<td>52.4 ± 3.8</td>
<td>47.6 ± 3.8</td>
<td>1.4 ± 0.7</td>
<td>15.7 ± 1.3</td>
<td>15.1 ± 0.9</td>
<td>15.4 ± 1.5</td>
</tr>
<tr>
<td>Linseed</td>
<td>47.5 ± 5.9</td>
<td>52.5 ± 5.9</td>
<td>2.8 ± 0.3</td>
<td>18.1 ± 2.6</td>
<td>14.3 ± 1.7</td>
<td>17.4 ± 2.0</td>
</tr>
<tr>
<td>Grape seed</td>
<td>45.7 ± 0.1</td>
<td>54.3 ± 0.1</td>
<td>2.9 ± 0.1</td>
<td>17.6 ± 0.5</td>
<td>16.6 ± 0.8</td>
<td>17.2 ± 0.4</td>
</tr>
<tr>
<td>Soybean</td>
<td>46.4 ± 1.5</td>
<td>53.6 ± 1.5</td>
<td>2.4 ± 1.2</td>
<td>17.3 ± 0.3</td>
<td>17.0 ± 0.3</td>
<td>17.0 ± 0.6</td>
</tr>
<tr>
<td>Corn</td>
<td>47.4 ± 7.0</td>
<td>52.6 ± 7.0</td>
<td>2.0 ± 0.4</td>
<td>17.6 ± 3.1</td>
<td>16.0 ± 1.1</td>
<td>17.0 ± 3.6</td>
</tr>
<tr>
<td>Sesame</td>
<td>41.2 ± 2.7f</td>
<td>58.8 ± 2.7f</td>
<td>8.6 ± 0.4f</td>
<td>15.8 ± 0.7</td>
<td>15.1 ± 1.1</td>
<td>19.3 ± 1.2f</td>
</tr>
<tr>
<td>Rapeseed</td>
<td>52.1 ± 4.1</td>
<td>47.9 ± 4.1</td>
<td>3.0 ± 0.5</td>
<td>15.0 ± 1.6</td>
<td>14.4 ± 1.7</td>
<td>15.6 ± 1.6</td>
</tr>
<tr>
<td>Rice bran</td>
<td>45.5 ± 3.2</td>
<td>54.5 ± 3.2</td>
<td>3.0 ± 1.1</td>
<td>18.1 ± 1.2</td>
<td>16.4 ± 0.2</td>
<td>17.0 ± 1.3</td>
</tr>
<tr>
<td>Safflower seedf</td>
<td>45.8 ± 2.5</td>
<td>54.2 ± 2.5</td>
<td>2.8 ± 1.5</td>
<td>17.4 ± 1.3</td>
<td>17.1 ± 0.5</td>
<td>16.9 ± 0.9</td>
</tr>
<tr>
<td>Olive</td>
<td>49.7 ± 4.3</td>
<td>50.3 ± 4.3</td>
<td>3.5 ± 2.5</td>
<td>15.2 ± 0.9</td>
<td>16.1 ± 0.6</td>
<td>15.5 ± 1.8</td>
</tr>
<tr>
<td>Sunflower seedf</td>
<td>55.2 ± 3.0f</td>
<td>44.8 ± 3.0f</td>
<td>2.0 ± 0.5</td>
<td>14.6 ± 1.5</td>
<td>14.1 ± 0.7f</td>
<td>14.1 ± 1.4f</td>
</tr>
</tbody>
</table>

\(a\)Values are presented as mean ± standard error \((n = 3)\).

\(b\)Percentage content of \(Z\)-isomers of lycopene relative to the total amount of lycopene isomers after the heating period.

\(c\)Total content of \(Z\)-isomers of lycopene.

\(d\)Sum of \(Z\)-isomers of lycopene other than 5\(Z\)-, 9\(Z\)-, and 13\(Z\)-forms.

\(e\)Oil with high oleic acid content.

\(f\)Statistically significant \((p < 0.05, \text{Student’s } t\text{-test})\) in each column.

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**Figure 2.** Efficiency of \(E\)-to-\(Z\) isomerization of lycopene in various vegetable oils. \((\text{all-}E)\)-Lycopene was heated at 100°C for 1 h (solid bars) and 3 h (shaded bars) in each oil. The efficiencies of isomerization to (A) \(Z\)-isomers of lycopene in total amount and (B) \((5Z)\)-lycopene were calculated by multiplying the percentage content of \(Z\)-isomers by remaining ratio of total amount of lycopene isomers without decomposition and by one-hundredth. Error bars indicate the standard error from triplicate samples. \(\ast\)Statistically significant \((p < 0.05, \text{Student’s } t\text{-test})\) in each group.
bioavailability, antioxidant capacity, and greater storage stability among the Z-isomers, was increased significantly. These findings are important, not only for the food, drink, and dietary supplement manufacturing industries, but also for daily cooking at home.

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The authors have declared no conflicts of interest.

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