Quantification of apo-lycopenals in food products and human blood plasma

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Abstract:
Consumption of tomato and tomato products has been associated with a reduction in risk for a number of cancers as well as heart disease. Tomato products contain a high level of the carotenoid lycopene, and researchers have hypothesized that lycopene or a metabolite of lycopene may be involved in modifying these disease processes. However, the metabolism of lycopene is poorly understood.

Oxidative breakdown products of lycopene have been recently observed in animal models. Apo-12'-lycopenal was found in lung tissue of smoking ferrets consuming lycopene. In addition, apo-8'-lycopenal and a compound presumed to be apo-12'-lycopenal have been reported in rats fed a lycopene-containing diet. Investigators have speculated that the enzyme beta-carotene oxygenase 2 (BCO2) is responsible for the formation of these oxidative products of lycopene.

A search of the literature reveals that apo-6'-lycopenal and apo-8'-lycopenal have been previously identified in raw tomatoes and tomato paste.

Our objectives were to determine whether:

1. Additional apo-lycopenals are present in tomatoes.
2. Apo-lycopenals are present in other lycopene containing foods.
3. Apo-lycopenals are present in the blood plasma of humans consuming a diet high in tomato products.
4. Quantify the levels of these products in foods and blood plasma.

Materials and Methods:
- Apo-lycopenals were synthesized using an ozonolysis method.
- Compounds were separated using reverse phase HPLC method and identified on a quadrupole time-of-flight hybrid mass spectrometer interfaced with the HPLC via an atmospheric pressure chemical ionization (APCI) source operated in negative ion mode.
- Foods were extracted using hexane:ethanol:acetonitrile (HEAT) mixture.
- Apo-6', apo-8', and apo-12'-lycopenal standards were used for quantitation. Lycopene was isolated from tomato paste and crystallized using an in-house method.

Table 1. Apo-lycopenals in common consumed lycopene containing foods

<table>
<thead>
<tr>
<th>Food</th>
<th>apo-6'-lycopenal*</th>
<th>apo-8'-lycopenal*</th>
<th>apo-10'-lycopenal*</th>
<th>apo-12'-lycopenal*</th>
<th>apo-14'-lycopenal*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roma Tomato</td>
<td>3.452</td>
<td>1.1</td>
<td>1.05</td>
<td>0.22</td>
<td>0.07</td>
</tr>
<tr>
<td>Grape Tomato</td>
<td>6.166</td>
<td>1.6</td>
<td>2.2</td>
<td>1.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Red Vine</td>
<td>3.778</td>
<td>3.5</td>
<td>4.3</td>
<td>2.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Peppered Tomato</td>
<td>0.37</td>
<td>0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Ruby Red</td>
<td>0.3</td>
<td>0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>0.37</td>
<td>0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Watermelon</td>
<td>0.3</td>
<td>0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Tomato Soup</td>
<td>1.1</td>
<td>0.33</td>
<td>0.4</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Tomato Juice</td>
<td>0.3</td>
<td>0.1</td>
<td>0.15</td>
<td>0.1</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Average 1.089 ± 0.12 (0.63 - 0.28) (0.73 - 0.12) (0.08 - 0.18) n.d

*Level was estimated by averaging apo-6'-lycopenal and apo-12'-lycopenal slopes.
**Level was estimated by using apo-12'-lycopenal equivalents.

- Levels reported are the average of duplicates for raw fruits and vegetables, and the average across three brand name products for processed tomatoes.
- Apo-lycopenals (and lycopene) were highest in tomato paste.
- The range of values for a particular apo-lycopenal species was 50% to 200% across different brands of a given product.

Figure 1. Chemical structures of all-trans lycopene and long chain apo-lycopenals observed after ozonolysis with ozone.

Figure 2. Standard curves of apo-12'-lycopenal, apo-8'-lycopenal, apo-6'-lycopenal, and lycopene.

Figure 3. Mass chromatograms showing lycopene and apo-lycopenals standards (A) vs. blood plasma extract (B) of a subject.

Figure 4. A comparison of the profile of lycopene and lycopene in tomato juice and blood plasma of individuals consuming tomato juice. Notice similarity.

Conclusions:
- To the best of our knowledge, this is the first report of apo-lycopenals observed in humans.
- An entire series of monoaldehyde lycopeneal (apo-6', 8', 10', 12') was observed in all foods tested. Apo-15'-lycopenal was not observed in food products or blood plasma tested.
- The level of apo-lycopenals in food products and blood plasma is roughly 1,000 times lower than the level of lycopene, but on par with levels of known carotenoid metabolites such as retinoic acid.
- The superior resolving power, sensitivity, and selectivity of HPLC-MS/MS, in combination with known standards, is essential for the detection and quantification of these compounds.

This research suggests that apo-lycopenals observed in blood plasma may be at least partly derived from the diet.

References:

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