Source, Structure & Function

Source
• β-Carotene is one of more than 600 carotenoids found in nature
• Natural food sources include yellow/orange fruits and vegetables (carrots, cantaloupes, apricots) and dark green leafy vegetables (kale, spinach, broccoli)

Structure
• Carotenoids are long hydrocarbons divided into:
  ➢ Carotenes (without oxygen)
  ➢ Xanthophylls (with oxygen)
• β-Carotene consists of a long chain (40 carbon atoms) of conjugated double bonds with a six-carbon ring on each end
• The long chain of conjugated double bonds is responsible for the orange color
• Exists as all-trans β-Carotene in nature

Function
• Most common carotenoids found in blood plasma are alpha-carotene, beta-carotene, and beta-cryptoxanthin (sources of provitamin A) and lycopene, lutein, and zeaxanthin (no activity)
• β-Carotene is the most abundant and efficient source of provitamin A in foods
• 50 carotenoids are known to have some provitamin A activity
β-Carotene: A Bright History

1800 - 1900

1907
Molecular Formula
Carotene
C₄₀H₅₆
(Willstatter & Mieg)

1900 - 1910

1929/30
β-carotene proven to be precursor of Vitamin A
(Moore)

1910 - 1920

1930/31
Chemical Structure
β-carotene
(Karrer)

1920 - 1940

1950
Synthesis of β-carotene
(Isner)

1940 - 1950

1966
β-carotene approved for Food
(FAO/WHO)

1950 - 1960

1954
Commercial Production
β-carotene
(Roche/DSM)

1960 - 1970

1979
β-carotene receives GRAS status in the USA
(FDA)

1970 - 1980

1980 - Present
Resources in Product Development 20+ Forms

1980 - Present

1987-93
β-Carotene 15% LCS

2000 - 2014
Introduction of β-carotene 5% LCS

2014 - Present
Clear Color (not turbid) carotenoids

FOR INTERNAL USE ONLY
Industrial Production

∀ β-Carotene is produced either by a chemical (nature identical) or a fermentation process (natural source)

- Commercially available since 1954 in crystalline form (Roche/DSM) and since 1960 (BASF)

- Roche’s original synthesis method was based on the Grignard reaction (enol-ether condensation) and followed the \( C_{19} + C_2 + C_{19} \) principle

- Today DSM is following the Wittig reaction and follows the \( C_{20} + C_{20} \) principle
# Dietary Reference Intakes (DRI)

DRIs are not currently established for β-Carotene, but research continues to support its role as a micronutrient.

## Vitamin A (Retinol)

<table>
<thead>
<tr>
<th>Age</th>
<th>Males &amp; Females</th>
<th>Pregnancy</th>
<th>Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>years</td>
<td>μg/day</td>
<td>μg/day</td>
<td>μg/day</td>
</tr>
<tr>
<td>1-3</td>
<td>300</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>4-8</td>
<td>400</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>9-13</td>
<td>600</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>14-18</td>
<td>900/700</td>
<td>750</td>
<td>1200</td>
</tr>
<tr>
<td>19+</td>
<td>900/700</td>
<td>770</td>
<td>1300</td>
</tr>
</tbody>
</table>

* Allowable levels of nutrients vary depending on national regulations and the final application

Source: IOM
Health Benefits of Beta-Carotene

• Dietary source of provitamin A that selectively converts to Vitamin A

• Antioxidant (radical scavenger and singlet oxygen quencher)

• Sun protection (UV-filter)

• After longterm intake (18 years), b-Carotene has a beneficial effect on some aspects of learning and memory
Carotenoids with Provitamin A Activity

6 mg β-Carotene \(^1\) correspond to 1 mg Retinol / Vit A

2 mg β-Carotene \(^2\) correspond to 1 mg Retinol / Vit A

Provitamin A active, but not allowed to claim

Vitamin A

\(\beta\)-Carotene

\(\beta\)-Apo-8ʻ-Carotenal

Retinol

\(^1\) According to the FAO/WHO. 1mg BC = 556.6 IU Vitamin A

\(^2\) According to the FDA. 1mg BC = 1667 IU Vitamin A
Provitamin A Pathway

**Beta-Carotene cleavage into 2 molecules of all-trans retinal**

- Two molecules of Vitamin A are generated from one molecule of beta-Carotene.
- Polymorphisms with a high prevalence in Caucasians (XY%) were found in the BCMO1 gene.
- Reduced activity of beta-Carotene mono-oxygenase due to polymorphisms leads to reduced formation of vitamin A.
- Beta-Carotene is a very safe form of Vitamin A since the body converts based on need. This prevents hypervitaminosis A.
- Excess Beta Carotene is stored in the fat tissues and liver.
Powerful Antioxidant

- β-Carotene reacts with reactive oxygen species (ROS) such as peroxo (ROO\cdot) and hydroxy (HO\cdot) radicals as well as singlet oxygen (\textsuperscript{1}O\textsubscript{2})

- Oxidation of carotenoids by ROS causes a loss in color

- Vitamin C and Vitamin E synergistically protect β-Carotene
Sun Protection

A meta-analysis including 7 clinical studies on the effect of β-Carotene on sunburn reduction revealed a significant protective effect (P= 0.0005) (Krutmann and Köpcke, 2007).

Chronic supplementation with βC results in SPF of ~ 2
Coloration

B-Carotene is a color additive exempt from certification and may be used in foods (21 CFR 73.95), cosmetics (21 CFR 73.2095), and drugs (21 CFR 73.1095)

<table>
<thead>
<tr>
<th>COLOR</th>
<th>SHADE</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-carotene</td>
<td>yellow to orange yellow</td>
<td>• good stability to light, heat and pH • vitamin C stable • survives retort • Kosher • has vitamin A activity • retort stable • has antioxidant activity</td>
<td>• susceptible to oxidation • not natural • not easy to use (have to prepare stock solution)</td>
</tr>
</tbody>
</table>
Protecting β-Carotene

The color of β-Carotene is stabilized in the presence of ascorbic acid
✓ Use 200-250mg/L to minimize color changes

The effect of natural antioxidants (vitamin C) on β-Carotene over time
# Forms Overview & Stability

<table>
<thead>
<tr>
<th>Water Dispersible Forms</th>
<th>Supplement Forms</th>
<th>Emulsions</th>
<th>Oil Based Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spray Dried</td>
<td>Beadlet</td>
<td></td>
<td>Suspension</td>
</tr>
<tr>
<td>Beadlet</td>
<td></td>
<td></td>
<td>Solution</td>
</tr>
</tbody>
</table>

- **crystal**
- **product forms**
- **in water**
- **in oil**

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**DSM**

**BRIGHT SCIENCE. BRIGHTER LIVING.**
**β-Carotene - Nature-Identical**

**Water Dispersible & Emulsion Product Forms**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>EINECS Number</th>
<th>Supplier Reference</th>
<th>Forfortification and coloration of water-based foods, instant products, beverages, puddings, confectionery and milk products. Color range:</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Carotene 1% CWS/M</td>
<td>50 03741.304</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>yellow.</td>
</tr>
<tr>
<td>Powder, cold water dispersible/medium chain triglycerides</td>
<td>50 03741.368</td>
<td></td>
<td>For fortification and coloration of water-based foods, instant products, beverages, puddings, confectionery and milk products. Color range: yellow.</td>
</tr>
<tr>
<td>β-Carotene 3% CWS/M</td>
<td>50 03636.304</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of water-based foods, instant products, beverages, puddings, confectionery and milk products. Color range: yellow.</td>
</tr>
<tr>
<td>Powder, cold water dispersible/medium chain triglycerides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 7% CWS</td>
<td>04 82285.231</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of beverages, puddings, confectionery and milk products. Color range: clear yellow.</td>
</tr>
<tr>
<td>Powder, cold water dispersible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 10% CWS</td>
<td>04 34825.268</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of beverages, soups, sauces, cereals and confectionery. Color range: yellow-orange to orange.</td>
</tr>
<tr>
<td>Beadlet**, cold water dispersible</td>
<td>04 34825.304</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 10% CWS/S</td>
<td>04 89999.304</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of beverages, soups, sauces, cereals and confectionery. Color range: yellow-orange to orange.</td>
</tr>
<tr>
<td>Beadlet**, cold water dispersible/starch</td>
<td>04 89999.341</td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 10% Emulsion Red</td>
<td>50 12538.147</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of juice and non-juice beverages, ice cream, yogurt and salad dressings. Color range: pink to strawberry red.</td>
</tr>
<tr>
<td>Liquid emulsion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 10% EM Yellow</td>
<td>50 02427.301</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of juice and non-juice beverages, ice cream, yogurt and salad dressings. Color range: yellow.</td>
</tr>
<tr>
<td>Liquid emulsion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Carotene 5% EM K</td>
<td>50 11256.311</td>
<td>JECFA*, Kosher Parve (OU) (BK), Halal</td>
<td>For fortification and coloration of juice and non-juice beverages, ice cream, yogurt and salad dressings. Color range: yellow.</td>
</tr>
<tr>
<td>Liquid emulsion</td>
<td>50 11256.356</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**β-Carotene - Nature-Identical**

**Oil Based Product Forms**

<table>
<thead>
<tr>
<th>Product Form</th>
<th>JECFA *, Kosher for Passover-Kitniot (BK), Kosher Parve (OU), Halal</th>
<th>Quantity</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-Carotene 30% FS</strong></td>
<td></td>
<td>1</td>
<td>04 27233.266</td>
<td>04 27233.311 04 27233.294 50 08735.175 50 08735.199 (Origin: France) For soft gelatin capsules. For fortification and coloration of fat-based foods. Color range: yellow.</td>
</tr>
<tr>
<td><strong>β-Carotene 30% FS Ph</strong></td>
<td></td>
<td>5</td>
<td>50 14387.294</td>
<td>For pharmaceutical preparations.</td>
</tr>
<tr>
<td>Fluid suspension</td>
<td></td>
<td>1</td>
<td>50 00238.311</td>
<td>For soft gelatin capsules. For fortification and coloration of fat-based foods. Color range: yellow.</td>
</tr>
<tr>
<td><strong>β-Carotene 30% FS/SF</strong></td>
<td></td>
<td>5</td>
<td>50 00238.311</td>
<td>For soft gelatin capsules. For fortification and coloration of fat-based foods. Color range: yellow.</td>
</tr>
<tr>
<td>Sunflower oil</td>
<td></td>
<td>20</td>
<td>04 66042.913</td>
<td>04 66042.313 For soft gelatin capsules. For coloration of popcorn, popping and frying oils. Color range: yellow.</td>
</tr>
</tbody>
</table>
**ß-Carotene - Nature-Identical Supplement Forms**

<table>
<thead>
<tr>
<th>Product</th>
<th>JECFA*</th>
<th>Code</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>BetaTab® 10% E</td>
<td></td>
<td></td>
<td>For effervescent tablets.</td>
</tr>
<tr>
<td>Beadlet**, tablet grade</td>
<td>5</td>
<td>04 34140.304</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>04 34140.368</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BetaTab® 20% S</td>
<td>JECFA*, Kosher Parve (OU) (BK), Kosher Ko, Halal</td>
<td>5</td>
<td>For direct compression tablets and hard gelatin capsules.</td>
</tr>
<tr>
<td>Beadlet**, tablet grade/starch</td>
<td>25</td>
<td>50 04004.304</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 04004.368</td>
<td></td>
</tr>
<tr>
<td>BetaTab® 20% S Ph</td>
<td>JECFA*, Kosher Parve (OU) (BK), Kosher Ko, Halal</td>
<td>25</td>
<td>For pharmaceutical preparations.</td>
</tr>
<tr>
<td>Beadlet**, tablet grade/starch</td>
<td></td>
<td>50 14352.368</td>
<td></td>
</tr>
</tbody>
</table>

---

*DSM BRIGHT SCIENCE. BRIGHTER*
Stock Solutions

✓ Recommended method for adding β-carotene to foods & beverages
✓ Applicable for water dispersible forms and oil based fluid suspensions
✓ Ensures complete dispersion of active prior to use
✓ Allows the user to volumetrically dose into the sample
✓ Standardizes concentration to 1mg of β-carotene per 1ml of solution

The Food Coloration Manual provides detailed preparation methods for each form
Specialty Forms for Foods & Beverages

Beta Carotene 15% LCS @ 20% DV Vitamin A

Beta Carotene 10%B is a cross linked beadlet
Beta Carotene - competitive environment

BASF / COGNIS
• Comprehensive product portfolio similar to DSM
• Backward integrated to crystal production
• Higher focus on feed than DSM, but Cognis acquisition has renewed focus on human nutrition

ALLIED
• Backward integration
• Human nutrition focus in EU, China, USA
• Portfolio similar to DSM and now includes Apocarotenal and β-Carotene emulsions

DIVIS
• Can synthesize crystals and forms
• Based in India
• Focused on export to EU and USA
• Considered lower end forms

Chinese producers (ZMC, NHU)
• Multipurpose and backward integrated plants
• Pricing for volume
• Very active in animal feed
• Sell via local distributors
References

- Choe and Min, Chemistry and Reaction of Reactive Oxygen Species in Foods, Journal of Food Science, Vol. 70, Nr.9, 2005, pg R142-159.
- Bonrath W et al., One Hundred Years of Vitamins - A Success Story of the Natural Sciences, Angewandte Chemie, 2012, 51, 12960-12990.