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Palm Nutraceutical Excellence

NATURAL MIXED-CAROTENE
with Highest Alpha-Carotene for Health
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The natural plant pigments that impart bright yellow, orange and red colors are carotenoids. Epidemiologists were thrilled by the observation that populations routinely consume carotenoid-rich fruits and vegetables were better protected against age-related diseases. The search for this component was narrowed down to beta-carotene as it is one of the most common dietary carotenoids.

However in the 1990s, supplementation of synthetic single form of beta-carotene intervention studies raised significant safety concern among the community as synthetic single form of beta-carotene posed potential health treats such as increased rate of lung cancer rather than protective effects. However, these negative effects were not observed from natural carotenoids derived from fruits and vegetable. In fact, these natural mixed-carotene / carotenoids confer synergistic health benefits that synthetic beta-carotene does not possess. Recent epidemiology studies have shown that high consumption of natural mixed-carotene (ie: alpha- & beta-carotene) rich sources such as fruits and vegetables are strongly associated with reduced risk of age-related diseases through preserving the telomere length, decreased risk of age-related macular degenerative disease (AMD), as well as promoting healthy blood sugar level and bone health.

EVTene™ is a natural mixed-carotene (mainly alpha-carotene and beta-carotene, in cis and trans forms) extracted and concentrated from palm fruits (Elaeis guineensis). Apart being a natural source of carotenes with nutritional value (provitamin A), the natural carotenes in EVTene™ may work synergistically to confer health beneficial properties. This paper will present compelling scientific information about natural mixed-carotene, alpha-carotene and their unique health attributes.
Fruits & Vegetables - The Natural Source of Carotenoids

“Eat A Rainbow” is a popular healthy eating quote but not many of us know the reasons of eating colorful fruits and vegetables. The vibrant colors of fruits and vegetables are not merely “eye candy”, they are natural carotenoids which are antioxidants that offer a number of health promoting properties. Carotenoids offer intense shadings of yellow, orange and red colors to plants and they are the most abundant natural pigments in the plant kingdom, with more than 700 identified carotenoids in nature [1].

There are two types of carotenoids, oxygen containing Xanthophylls such as lutein and zeaxanthin; and pure hydrocarbon Carotenes are such as alpha-carotene, beta-carotene and lycopene.

Interestingly, some carotenes like alpha-carotene, beta-carotene, and gamma-carotene are provitamin A carotenoids, which can be converted to vitamin A when there is a deficiency in our body to support eye health.

Among all provitamin A carotenoids, beta-carotene is the most abundant dietary carotenoid [2]. Historically, the image of β-carotene has been projected to the forefront through indirect observations from several major population studies. However, β-carotene was unfortunately, sent into a tailspin following negative findings from a few large β-carotene intervention trials.
The Beta-Carotene Debacle

In the 1990s, three β-carotene intervention trials - CARET (Beta-Carotene and Retinol Efficacy Trial), PHS (Physician's Health Study) and ATBC (Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study) were carried out. These studies involved almost 66,000 humans to specifically confirm the beneficial effects of β-carotene. Surprisingly, the results of these studies were largely contradictory to the anti-cancer properties hypothesized for β-carotene, as shown below:

1. CARET (Beta-Carotene and Retinol Efficacy Trial)

EFFECT OF A COMBINATION OF THE BETA CAROTENE AND VITAMIN A ON LUNG CANCER AND CARDIOVASCULAR DISEASE

Abstract Background. Lung cancer and cardiovascular disease are major causes of death in the United States. It has been proposed that carotenoids and retinoids are agents that may prevent these disorders.

Methods. We conducted a multicenter, randomized, double-blind, placebo-controlled primary prevention trial — the Beta-Carotene and Retinol Efficacy Trial — involving a total of 18,314 smokers, former smokers, and workers exposed to asbestos. The effects of a combination of 30 mg of beta carotene per day and 25,000 IU of retinol (vitamin A) in the form of retinyl palmitate per day on the primary end point, the incidence of lung cancer, were compared with the placebo group. There were no statistically significant differences in the risks of other types of cancer. In the active-treatment group, the relative risk of death from any cause was 1.17 (95 percent confidence interval, 1.03 to 1.33); of death from lung cancer, 1.46 (95 percent confidence interval, 1.07 to 2.00); and of death from cardiovascular disease, 1.26 (95 percent confidence interval, 0.99 to 1.61). On the basis of these findings, the randomized trial was stopped 21 months earlier than planned; follow-up will continue for another 5 years.

Conclusions. After an average of four years of supplementation, the combination of beta carotene and vita-

The CARET study was prematurely terminated when increased incidence of mortality from lung cancer became obvious among the subjects supplemented with single isoform of β-carotene.
The ATBC study also reported similar increased incidences of lung cancer with $\beta$-carotene consumption.

The PHS study found no beneficial effects – neither negative nor positive with $\beta$-carotene supplementation.

It is also worthwhile to note that these three studies were carried out with synthetic and single form of $\beta$-carotene \([3-5]\). The idea that single form of carotene such as $\beta$-carotene alone out of 700 carotenoids in nature is the “magic bullet” has caused many of us ‘miss the boat’ as far as health beneficial effects of carotenoids is concerned. The most common carotenoids in our diet are alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein, zeaxanthin and lycopene. These carotenoids are important to maintain optimum health functions in relation to their antioxidant activities and or other non-antioxidant activities, such as promoting eye health and skin nutrition.
The Value of Other Carotenoids

β-carotene was thought to be the most powerful carotenoid when it was first discovered. However, with the growing body of scientific evidence, the market has evolved to natural multi-carotenoids extracted from fruits, vegetables or even flowers. For example, lutein and zeaxanthin from marigold, lycopene from tomato and natural alpha-carotene and beta-carotene from palm fruits.

These natural carotenoids provide synergistic health effects, and additional biological advantages than single isomer of carotenoid. For example, in a 12-year follow up study conducted in Japan, it is found that high serum level of total carotenes especially α-carotene, β-carotene and lycopene are linked with reduced risk for cardiovascular disease mortality among Japanese aged 39 to 80 years [6]. Another two cohort studies conducted in the US, involving a 12-year follow up study with approximately 120,000 study participants reveals significant reduction in the risk of lung cancer with high consumption of several carotenes such as alpha-carotene and lycopene [7].

In addition, high consumption of alpha-carotene together with beta-carotene demonstrates decreased prevalence of atherosclerosis in carotid and femoral arteries as well as 5-year incidence of arteriosclerotic lesions in carotid arteries among men and women population aged 45 to 65 years [8].

These studies further highlight the importance of “natural and wholesome” antioxidant and carotenoid products for human health.
Some foods are particularly rich in alpha-carotene, and alpha-carotene often coexists with beta-carotene in fruits and vegetables. Although the vitamin A activity of alpha-carotene is only half of beta-carotene [9], study has shown that alpha-carotene possesses stronger antioxidant efficacy than beta-carotene in phosphatidyl choline vesicles (cellular organelles that transport nutrient into tissues), and thereby minimizing free radical-mediated peroxidative damage against cell membrane in vivo [10].

When comparing to beta-carotene, research demonstrates that alpha-carotene shows ten times stronger protective effects against certain cancer such as human neuroblastoma cells (ie: a type of cancer that affects early stages of neuronal cells development in infants or young children) in a dose-dependent manner [11]. In addition, alpha-carotene suppresses the initiation of cancer formation in liver, lung and skin more effectively in mice [12].

A 14-year follow up epidemiology study demonstrates inverse association between high consumption of alpha-carotene from fruits and vegetables and decreased risk of death from cardiovascular disease and cancer among US adults aged 20 years and older [13]. Several epidemiologic studies have shown that high consumption of alpha-carotene from natural foods and dietary supplementation is inversely associated with ovarian cancer, especially among postmenopausal women [14]. Additionally, high blood level of alpha-carotene shows significant inverse relationship with the risk of cervical dysplasia among Japanese women aged 55 and above [15].

In addition, a recent study evaluated the impact of nutritional supplements which include carotenoids (alpha-carotene, beta-carotene, beta-crytoxanthin and lycopene) and vitamins on optimal phenotypic flexibility (ie: ability to respond and adapt to physiological changes) followed by a nutritional challenge test (NCT) that consists of high fat diet among 36 overweight or obese male subjects. The results show that alpha-carotene is a crucial micronutrient for maintaining phenotypic flexibility. Alpha-carotene demonstrates inverse relationship with proinflammatory markers, hence alpha-carotene is believed to modulate or support immune health [16].

While Alpha-Carotene is more potent than Beta-Carotene, they work synergistically to confer the optimum carotenoid protection.
Dietary intake of natural Mixed-Carotene or Carotenoids (i.e. combination of alpha-carotene, beta-carotene and other carotenoid compounds) from fruit and vegetables have shown better health promoting properties. As a matter of fact, recent cohort studies have shown that high intakes of mixed-carotene increase telomere length, which is strongly associated with reduced risk of age-related diseases. Additionally, studies have also shown that high consumption of carotenoids attenuates the risks of developing type 2 diabetes and increases bone mineral density. The summary of these cohort studies are shown in the next few pages:
Telomeres are specialized structures at the end of the chromosomes to protect the loss of human’s genetic data during cell division. The length of the telomere shortens each time after cell division and the shortening process is associated with accelerated aging, higher risk of cancer development and death. 3660 participants aged 20-year-old and above US adults were recruited in the 1999-2002 National Health and Nutrition Examination Survey (NHANES). The concentration of plasma carotenoids (alpha-carotene, beta-carotene, beta-cryptoxanthin, combined lutein/zeaxanthin and trans-lycopene) were measured. DNA samples were extracted from whole blood and the leukocyte telomere length (T/S ratio) were determined.

Additionally, when comparing to the lowest carotenoid (alpha-carotene, beta-carotene and beta-cryptoxanthin) quartiles, the telomere length increased from 5-8% in the highest carotenoid quartiles cohort. Hence, this study suggests that high consumption of mixed-carotene rich food increases telomere length [17].

From the results, it was found that plasma blood level of alpha-carotene, beta-carotene and beta-cryptoxanthin were significantly associated with 1.76%, 2.22% and 2.02% longer telomeres respectively [17].
Minimizes Risk of Age-Related Macular Degeneration

Photo oxidative stress is a phenomenon where reactive oxygen species (ROS) is produced when there is a light exposure that might lead to damaged biomolecules (DNA, hormones, enzymes, and minerals) and instability of light-exposed tissues such as eyes. AMD is an irreversible blindness due to photooxidative stress.

Published in the *Journal of the American Medical Association* (JAMA), this long-running prospective cohort involves more than 100,000 subjects - 63443 women from Nurses’ Health Study (NHS) and 38603 men from Health Professionals Follow-up Study (HPFS) for 26 and 24 years respectively. The plasma carotenoids were predicted from food intakes and repeated food frequency questionnaires at baseline.

It was found that high intake of bioavailable mixed-carotene complex, particularly alpha-carotene, beta-carotene, lutein and zeaxanthin was inversely associated with AMD [18].

As such, this compelling study suggests that protection against photooxidative stress is related to antioxidative properties of the macular carotenoids (alpha-carotene, beta-carotene, lutein and zeaxanthin) [18].
Type 2 diabetes occurs when there are elevated levels of glucose or fatty acids that induce production of free radicals-mediated oxidative stress or insulin insensitivity. A study conducted in Netherlands where 37,846 men and women of the European Prospective Investigation into Cancer and Nutrition were recruited and followed up for a mean of 10 years. The participants’ dietary intakes of α-carotene, β-carotene, β-cryptoxanthin, lycopene, lutein and zeaxanthin, and sum of the carotenoids were assessed using food frequency questionnaire [19].

A 10-year follow-up study conducted among 1073 males and females age between 30 to 79 year-old from Japan showed inverse association between serum carotenoids (alpha-carotene, beta-carotene, beta-cryptoxanthin, zeaxanthin, lutein and lycopene) and the risk of type 2 diabetes development. Interestingly, the reduced risk of type 2 diabetes was not only observed in non-smokers and non-drinkers, but also in light drinkers [20].
Bone mineral density (BMD) indicates an individual’s risk of osteoporosis, where high BMD reduces the risk of bone fracture and vice versa. A cross-sectional study reveals that high concentration of serum carotenoids is positively correlated to higher BMD in middle-aged and elderly Chinese adults, especially in women. This study recruited 1898 women and 933 men aged 50-75 years and the follow-up study was done after a mean interval of 3.1 years [21].

The results again demonstrate that the synergistic effect of high level of alpha-carotene, lycopene and beta-cryptoxanthin are associated with increased BMD at most skeletal sites in women. By contrast in men, only high serum alpha-carotene was significantly associated with increased BMD at all sites except for lumbar spine [21].

Summary:

These peer-reviewed studies (i-iv) reveal the importance of dietary intake of natural mixed-carotene from natural carotenoid sources such as palm fruits and carrots for healthy aging and protection. All these different forms of carotenoids work synergistically to confer optimum health.
EVTene™ is a natural mixed-carotene derived from palm fruits. Palm fruits (Elaeis guineensis) is the world’s richest natural plant source of carotenes in terms of retinol (provitamin A) equivalent. It contains about 15 to 300 times as many retinol equivalents as carrots, leafy green vegetables, and tomatoes. There are 4 main commercial sources of carotenes, namely synthetic beta-carotene from petroleum, fermentative beta-carotene from fungus, algae beta-carotene and palm mixed-carotene complex.

Synthetic beta-carotene is commonly known as “natural identical beta-carotene”, it is chemically synthesized and contains only trans-beta-carotene. Likewise, beta-carotene derived from yeast fermentation and algae are predominantly contain ONE single carotene only- with more than 96% beta-carotene.

Cis carotene-isomer is a stronger antioxidant as it has been proven that cis-isomer quenches free radicals more effectively than trans-isomers [22]. In other words, natural carotene sources show stronger antioxidative activity compared to synthetic carotene sources.

Another unique attribute of EVTene™-palm mixed-carotene complex is that it has similar carotene composition as found in carrots, with approximately 33% of alpha-carotene, 65% beta-carotene and 2% of other carotenes (e.g. γ-carotene, lycopene).
### Comparison Table - Commercial Carotene Products

<table>
<thead>
<tr>
<th>Commercial Carotenoid Products</th>
<th>Palm Mixed-Carotene Complex (EVTene™)</th>
<th>Algae B-carotene</th>
<th>Fermentative B-carotene</th>
<th>Synthetic B-carotene</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source</strong></td>
<td>Crude palm oil (<em>Elaeis guineensis</em>)</td>
<td>Algae (<em>D. salina</em>)</td>
<td>Fungus (<em>B. trispora</em>)</td>
<td>Petroleum</td>
</tr>
<tr>
<td><strong>Composition</strong></td>
<td>33% α-carotene 65% β-carotene 2% other carotenoids (mixed-carotene complex)</td>
<td>&gt; 96% β-carotene (predominantly a single beta-carotene source)</td>
<td>&gt; 98% β-carotene (predominantly a single beta-carotene source)</td>
<td>100% β-carotene (single β-carotene source)</td>
</tr>
<tr>
<td><strong>α-carotene</strong></td>
<td>Highest level of α-carotene (33 to 35%)</td>
<td>Negligible level of α-carotene</td>
<td>Negligible level of α-carotene</td>
<td>No α-carotene</td>
</tr>
<tr>
<td><strong>Cis and trans isomers</strong></td>
<td>Cis and trans</td>
<td>Cis and trans</td>
<td>~ 100% trans</td>
<td>100% trans</td>
</tr>
<tr>
<td><strong>Ratio &amp; Composition of Carrot Carotenoids</strong></td>
<td>Similar</td>
<td>Different</td>
<td>Different</td>
<td>Different</td>
</tr>
</tbody>
</table>
Conclusion

Not all carotenes are created equal. Obviously, there are clear differences between single and synthetic carotene compound and natural mixed-carotene. Each carotenoid isomer in the natural mixed-carotene works synergistically to provide the unique biological health benefits associated with consuming fruits and vegetables. With increasing scientific evidences show that alpha-carotene is a stronger antioxidant compared to beta-carotene, it is believed that the synergism of both alpha-and beta-carotene offer stronger health beneficial properties. Apart from that, with heightened health concerns, consumers these days are increasingly emphasizing on the naturalness and origin of the products for a clean label. In this regard, consumers, retailers and dietary supplement manufacturers are progressively searching and sourcing for a true natural mixed-carotene complex.

ExcelVite’s EVTene™ - natural palm mixed carotene complex is the carotenoid of choice for manufacturers and consumers.

EVTene™ is extracted from sustainably-sourced non-GMO palm fruits. Therefore, EVTene™ is not only a “Eco-friendly Whole Food Supplement”, but also a TRUE mixed-carotene with valuable health benefits!
References


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