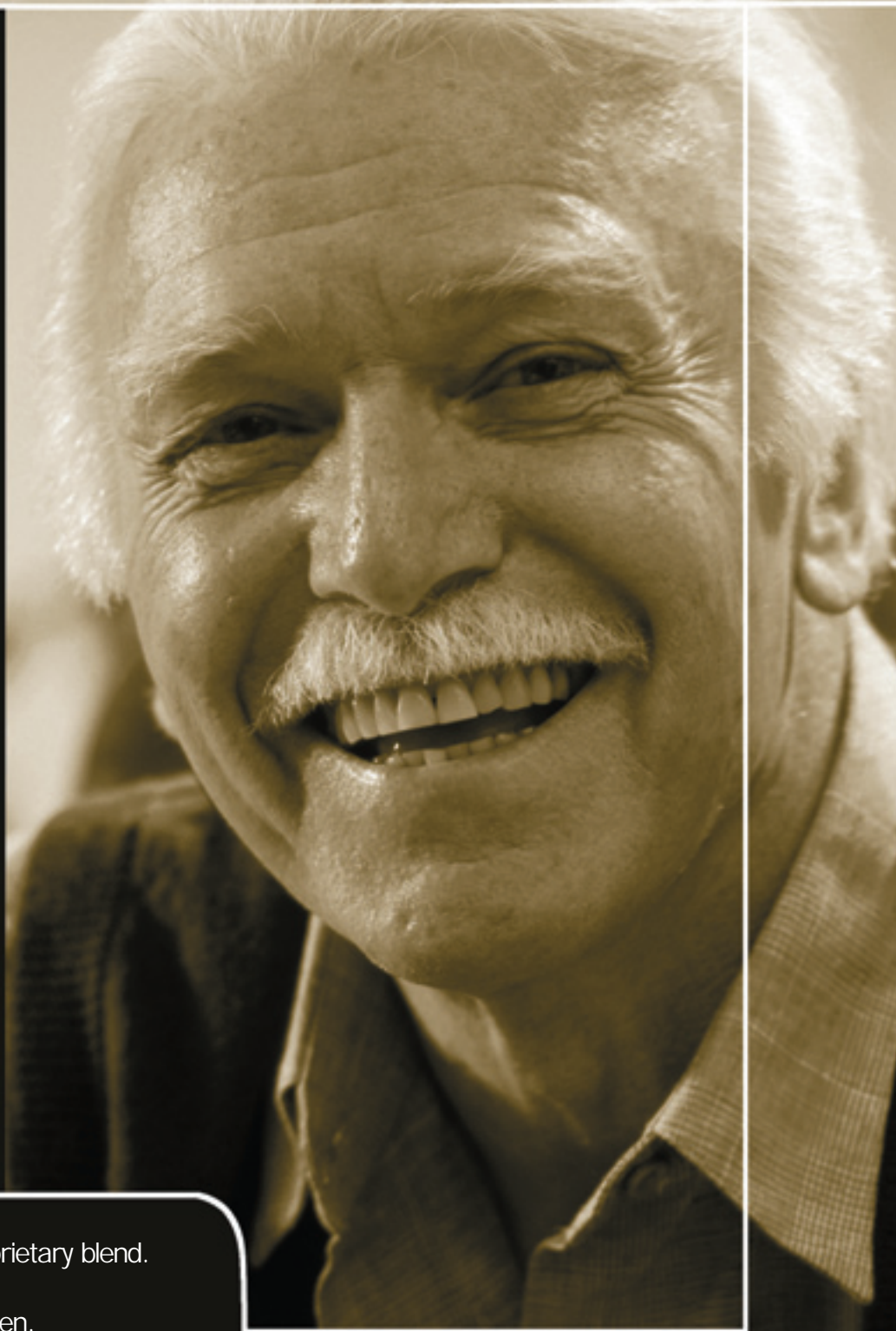




# Pollen Power for the Prostate

The health of the prostate is something most men never think about ... until they're forced to. So the fact that so many men are willing to take drugs with known, serious side effects, or to even undergo surgery, attests to how common, how unpleasant, and how *personal* prostate health concerns can be. Saw Palmetto, Stinging Nettle, *Pygeum africanum*, Beta-sitosterol, and other herbal formulas have become widely known as natural ways to support the health of the prostate, but research shows they don't live up to many men's expectations. And in some cases - like Saw Palmetto - it's not even certain that they're of any help at all.

**Prostaphil-2®** may change all that. Used by men for two generations in Europe, the power of this proprietary pollen extract from Sweden is backed by numerous clinical and experimental studies. Research shows that this defined pollen extract can **support a healthy prostate**, in ways that the more common prostate herbals don't. Look into **Prostaphil-2®**. You may just find that you sleep better at night.



- Unique proprietary blend.
- Clinically proven.
- Safer and more effective than Saw Palmetto.





## IS YOUR BETA CAROTENE TOXIC!

The version in your multivitamin may be hazardous to your health!

**Beta-carotene**, the main pigment which gives the orange color to sweet potatoes and carrots, is well-known and well-represented in the daily supplement regimen of nearly all health-conscious North Americans. For many years, this nutrient was thought to be simply a source of **provitamin A** -- that is, a substance from which the body could make vitamin A itself (retinol). But all this began to change in the early 1980s, when a powerful, large-scale epidemiologic study<sup>1</sup> revealed an astonishing connection between intake of this carotenoid and lung cancer: **men who took in the greatest amount of carotenes were seven to eight times less likely to develop lung cancer than those who took in the least** -- a result unaffected by their varying intake of retinol or other nutrients. This result represented a risk reduction so great as to indicate that **smokers with the highest carotene intakes had the same relative risk for lung cancer as non-smokers** in lower-intake groups. Since 1977, 53 of 135 epidemiological studies have found **significant reduction of risk for cancer from b-carotene**, measured as dietary intake or plasma levels; fully half of the remainder also found risk reductions, but the results were not strong enough to be considered statistically significant.

This result was in line with evidence accumulated before and since on the role of b-carotene as a potent **antioxidant** (especially as a **quencher of singlet oxygen (O<sub>2</sub>)**) with **anticarcinogenic** powers. Extensive experimental work in lab animals<sup>5</sup> and isolated cells<sup>6</sup> indicated that **b-carotene can prevent the development of cancer, and even stop the growth of existing cancerous cells**. Cellular studies found that b-carotene could **decrease transformation of benign tumors to malignant cancers, increase the cell-to-cell communication normally lost by cancer cells, prevent UV damage, reduce chromosome**

**instability** induced by viruses, **kill tumor cells** in some cancer lines, and even **induce differentiation**, turning some cancer cells into normal, healthy ones again<sup>6</sup>. Excitement built, and double-blind, randomized, placebo-controlled trials in men at very high risk for lung cancer were initiated: the **Alpha-Tocopherol and Beta-Carotene (ATBC)** Cancer Prevention Study, and the **Carotene and Retinol Efficacy Trial (CARET)**.

### Unbelievable Results

The results came as a complete surprise. The trials<sup>7,8</sup> were called off early in 1995 and 1996, because preliminary analysis not only failed to find any improvement in lung cancer rates in the active groups, there was a **non-significant suggestion of an increase in lung cancer rates!** And while an analysis published as a press release in the New England Journal of Medicine declared that another large b-carotene trial -- the Physicians' Health Study -- had found no such risks, it found no benefit either.

On the one hand, **the excess cancer incidence was not statistically significant**, so there is the temptation to ignore the results until better data are available; but when two separate, large-trials seem to show the same increased risk, caution is in order. So what might be going on here?

### Flawed Trials

Actually, probably several things at once. For one thing, there is the **high-risk populations used**: ATBC and CARET deliberately chose to study men who were long-term smokers (and, in ATBC's case, also asbestos workers!) in order to get a clear therapeutic result. But it now appears from new human trials that, while b-carotene can prevent the cells from becoming cancerous (initiation)<sup>9</sup>, it may not be able to halt the spread of existing cancers (progression)<sup>10</sup>. Subjects at very high risk **may thus have already have had early-stage cancer** when the trial began, and b-carotene may not affected them.

Worse, it would appear that **smoking may make b-carotene a health hazard when it is given alone**. This is because the teamwork involved in antioxidant

biochemistry is upset by the massive doses of free radicals to which smoking exposes smokers' lungs and bodies. When a free radical is quenched by an antioxidant, the "lonely electron" is given a mate by the antioxidant molecule. In the process, however, *the antioxidant itself becomes a free radical*. Progress is only possible because the new free radical is less toxic than the old one. The body's antioxidant defenses are designed to work as a team, with one antioxidant quenching a free radical, and then being itself quenched by another antioxidant in turn, leading to progressively less toxic byproducts, until vitamin C -- the final acceptor -- is finally flushed out through the kidneys. It's like a game of "hot potato," with the potato cooling off with each pass.

In smokers, however, this process is interrupted, because **smoking rapidly depletes other antioxidants**. As a result, giving b-carotene *alone* to smokers may have resulted in a high level of toxic b-carotene "radicals" accumulating in the lungs from contact with cigarette smoke, with no vitamins C and E available to detoxify them<sup>11</sup>. Interestingly, later analysis of the ATBC and CARET data suggested **no risk, or even a protective effect, for b-carotene in light smokers** even as heavy smokers seemed to show increased risk<sup>2,3</sup>. A more recent trial using a combination of antioxidants<sup>4</sup> found that **b-carotene in combination with selenium and vitamin E significantly cut cancer risk**; better results might have been expected had vitamin C been included. In fact, a new Physicians' Health Study<sup>13</sup> is now under way which will use a combination of E, C, b-carotene, and a multivitamin against cancer and cardiovascular disease; we await the results with great optimism. In food, of course -- the source of b-carotene in the original epidemiological studies -- **b-carotene always comes along with vitamins C and E**; supplement programs should follow this pattern.

The ATBC subjects' high intake of alcohol may also have been a factor, because **high-dose alcohol interacts dangerously with b-carotene** because of their use of common liver detoxification

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pathways<sup>12</sup>. Nearly all of the apparent excess lung cancer in the CARET group was in a subpopulation with high alcohol intake<sup>2</sup>; and, similarly, the risk of cancer appeared to be higher in regular drinkers than non-drinkers in ATBC<sup>3</sup>, although this finding has recently been disputed<sup>16</sup>.

### The Wrong Molecule

But perhaps the most disastrous failure in the design of the controlled trials is that they used the wrong **b-carotene**. For most supplements, whether they are derived from cellular “factories” or pharmaceutical ones makes no difference to their chemical structure or biological activity; natural versus synthetic vitamin E is one of a very few exceptions to the rule.

Crucially, **b-carotene** is another.

The **b-carotene** used in CARET and ATBC was **synthetic b-carotene**, which is *chemically different* from the **b-carotene** found in food. **Synthetic b-carotene** is entirely in the “*trans*” form; by contrast, **natural b-carotene** is a mixture of *trans* and *cis* isomers. Many health-conscious people are by now aware of the great difference between the *trans* fatty acids in partially hydrogenated vegetable oils and the *cis* fats in natural EFA sources. In *trans* bonds, the hydrogens attached to two adjoining double-bonded carbons are on opposite sides of the molecule, giving it a flat molecular shape. *Cis* isomers, by contrast, have one double bond in which the two carbons’ hydrogens are on the *same* side of the molecule’s backbone; and since the two hydrogens repel one another (because they both carry a positive charge -- an effect rather like two magnets aligned at their “north” end), the molecule is bent at this point (see **Figure 3**).

### Synthetic b-carotene: Not an Antioxidant

We do not want to bore you with detailed chemistry, so let us get to the point: while *trans* **b-carotene** can still be used to make vitamin A, **only the *cis* form is directly useful as an antioxidant in the body!** In one trial<sup>14</sup>, subjects were given either natural **b-carotene** supplements from the algae *Dunaliella bardawil*, synthetic **b-carotene**, or a placebo, and levels of a

marker of **lipid peroxidation** (free radical damage to cell membranes, LDL, etc) were measured. Not only did the all-*trans* **b-carotene** fail to provide any measurable antioxidant protection compared to the dummy pill, but **the group receiving synthetic b-carotene actually had 13% more markers of free radical damage than the placebo group!** Although this result was not statistically significant, it contrasts sharply with the group receiving **the natural-source supplement, which delivered a 76% reduction in peroxidation markers**. Similar results were reported in a test-tube study by Levin and Mokady<sup>26</sup>.

This lack of antioxidant ability is bad enough in itself -- suggesting, as it does, that the synthetic **b-carotene** administered to the ATBC and CARET smokers could not have helped them -- but further investigation suggests a more chilling conclusion. First is the possibility that **synthetic b-carotene supplements may actually deplete the body of the natural *cis* isomer**. This is because both forms of **b-carotene** use the same absorption pathway, which only allows a limited transport of this carotenoid at a given time<sup>15</sup>, so that large-dose **synthetic b-carotene supplements may actually inhibit absorption of the natural *cis*- form of b-carotene**. Ironically, in fact, the liver appears to transport the *trans* form *more* efficiently than the *cis* isomer<sup>18</sup>, so that taking in one unit of synthetic **b-carotene** might prevent more than one unit of the

active antioxidant isomer from being absorbed. To understand the problem, think of a group of prank callers tying up telephone lines of an organization, preventing legitimate callers from making contact. Now imagine that there are more pranksters than callers with real reasons for trying to get through. *Now* imagine that the lines being tied up are used by 9-1-1 emergency operators ...

Some have speculated that the absorption inhibition issue could be even more serious, since an overload of synthetic **b-carotene** might be expected to also reduce uptake of other carotenoids such as **lycopene, lutein, and a-carotene**. One preliminary report on the ATBC subjects paradoxically reported that lutein was, indeed, depressed in those receiving synthetic **b-carotene**, but that some other carotenoids were actually *increased* in serum<sup>19</sup>. Several other reports, however, have shown no association between intake of the artificial supplement and levels of any carotenoid other than **b-carotene** itself<sup>23, 24, 25</sup>.

### Artificial b-carotene Damages Genes

An even greater reason to stay away from the use of synthetic **b-carotene** supplements was given by a recent study which found that, while both natural and synthetic **b-carotene** protected immune cells from damage by gamma radiation, **synthetic b-carotene itself caused chromosome damage in these cells**, with the number of damaged cells increasing with the dosage<sup>17</sup>! By contrast, natural **b-carotene** caused no such spontaneous damage. In the same study, **natural b-carotene protected cells from DNA cross-linking** induced by the antibiotic **mitomycin C**, which the **synthetic form was not reported to do**.

A small trial reported just before the ATBC alarm sounded shows that these are not just theoretical concerns. The trial was conducted patients with precancerous cells in their stomachs. It assigned the patients to receive one of three supplements: natural **b-carotene**, synthetic **b-carotene**, or a placebo. When the researchers looked at the results, they found that **only the natural supplement had reduced the abnormal cellular development**<sup>21</sup>.



Thus, the synthetic **β-carotene** used in ATBC, CARET, and most **β-carotene** supplements available on the market appear to simultaneously inhibit the absorption of beneficial *cis* **β-carotene**, and to be themselves possible carcinogens. In sum, **synthetic β-carotene supplements may be worse than useless: they may actually be harmful**, especially to high-risk populations like those in the large trials. The only reason we can see for the use of the artificial supplement in CARET

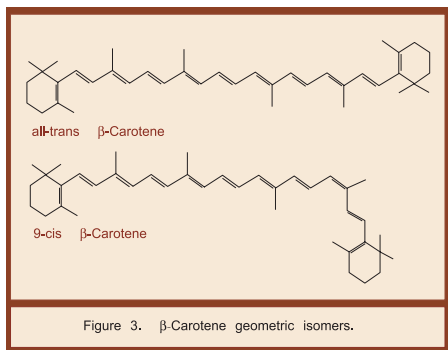


Figure 3. β-Carotene geometric isomers.

and ATBC is its low cost; in retrospect, as a letter to the New England Journal of Medicine put it, the use of this supplement “is neither hard to understand nor easy to forgive.”<sup>22</sup>

### Choosing the Right β-Carotene

To recap: there are many reasons to believe that the results of the large-scale trials of **β-carotene** were the results of flawed design, and that we should trust the extensive epidemiological, animal, and cellular evidence that **β-carotene can prevent the development of cancer**. The evidence strongly suggests that a central flaw in the ATBC and CARET trials may have been the use of synthetic (all-*trans*) supplements. Fortunately, the problem of synthetic **β-carotene** is not inescapable: while most multivitamins, ACES combinations, and stand-alone **β-carotene** supplements still use the artificial molecule, **supplements are available which contain natural β-carotene exclusively**, usually derived from marine algae. These supplements deliver **β-carotene** in the natural form, with the vital *cis* isomers present. But we have to learn from the trials’ other mistakes as well. It is important to **ensure that you are also taking a spectrum of antioxidants** with your **β-carotene**, especially vitamins C and E. It may also be important to **avoid excessive consumption of alcohol** -- a wise policy in any case. And, most important of all -- for your own sake, **quit smoking**.

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Your body can only absorb fat-soluble vitamins (like CoQ10, beta-carotene, tocotrienols, and lycopene) when they're dissolved in fat. To get maximum benefits make sure there's a little fat in the meal when you swallow the pill-- and never take them on an empty stomach!