



## Sportsmen's Edge *Medical References*<sup>®</sup>

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**More at [www.astaxanthin.org/references.htm](http://www.astaxanthin.org/references.htm)**

## ATHLETIC PERFORMANCE REFERENCES

### ASIAN GINSENG or American Ginseng (*Panax Quinquefolius*) 80-100 mg Standard Extract

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**BPH/PROSTATITIS/PROSTATE CANCER/ANTIOXIDANT – 30mg/day**

**PDR REFERENCE**

**Lycopene**

## **TRADE NAMES**

Lycopene (Nature's Answer)

## **DESCRIPTION**

Lycopene is a member of the carotenoid family of chemical substances. Lycopene, similar to other carotenoids, is a natural fat-soluble pigment (red, in the case of lycopene) found in certain plants and microorganisms, where it serves as an accessory light-gathering pigment and to protect these organisms against the toxic effects of oxygen and light. Lycopene may also protect humans against certain disorders, such as prostate cancer and perhaps some other cancers, and coronary heart disease.

Carotenoids are the principal pigments responsible for the colors of vegetables and fruits (see Beta-Carotene and Lutein and Zeaxanthin). Lycopene is responsible for the red color of red tomatoes. In addition to tomatoes (*Lycopersicon esculentum*) and tomato-based products, such as ketchup, pizza sauce, tomato juice and tomato paste, lycopene is also found in watermelon, papaya, pink grapefruit and pink guava. Processed tomato products are more available dietary sources of lycopene than fresh tomatoes. The average daily intake of lycopene is approximately 25 milligrams, with 50% of this in the form of processed tomato products.

Lycopene is an acyclic isomer of beta-carotene. Beta-carotene, which contains beta-ionone rings at each end of the molecule, is formed in plants, including tomatoes, via the action of the enzyme lycopene beta-cyclase. Lycopene is a 40 carbon atom, open chain polyisoprenoid with 11 conjugated double bonds. The structural formula of lycopene is represented as follows:

## Lycopene

All-trans lycopene is the predominant geometric isomer found in plants. *Cis* isomers of lycopene are also found in nature, including 5-*cis*, 9-*cis*, 13-*cis* and 15-*cis* isomers. Lycopene found in human plasma is a mixture of approximately 50% *cis* lycopene and 50% all-*trans* lycopene. Lycopene in processed foods, is mainly in the form of the *cis*-isomer.

Lycopene is a lipophilic compound and is insoluble in water. Lycopene is also known as psi-carotene. Its molecular formula is  $C_{40}H_{56}$  and its molecular weight is 536.88 daltons. In contrast to beta-carotene, lycopene has no vitamin A activity and thus is a nonprovitamin A carotenoid.

## **ACTIONS AND PHARMACOLOGY**

### **ACTIONS**

Lycopene may have anticarcinogenic and antiatherogenic activities.

The intake of tomato-based foods, especially processed tomato products, is associated with a significantly lower risk for prostate cancer, and also appears to be associated with a lower risk for lung cancer. The mechanism of the possible anticarcinogenic activity of lycopene is not well understood, but there are a few hypotheses. Cancer, as well as several other chronic diseases, is linked to oxidative stress. *In vitro* studies have demonstrated that lycopene has the highest antioxidant activity of all the carotenoids. It has the ability to quench singlet oxygen (more so than beta-carotene), to trap peroxy radicals, to inhibit the oxidation of DNA, to inhibit lipid peroxidation, and in some studies, to inhibit the oxidation of low-density lipoprotein (LDL).

### **MECHANISM OF ACTION**

Non-antioxidant mechanisms have also been proposed. Failure of cell signaling

stimulate gap junction communication between cells. It is speculated that lycopene may suppress carcinogen-induced phosphorylation of regulatory proteins such as p53 and Rb antioncogenes and stop cell division at the G<sub>0</sub>-G<sub>1</sub> cell cycle phase. One researcher has hypothesized that lycopene-induced modulation of the liver metabolizing enzyme cytochrome P450 2E1 may be the underlying mechanism of protection against carcinogen-induced preneoplastic lesions in the rat liver. Lycopene may also reduce cellular proliferation induced by insulin-like growth factors. There is some preliminary *in vitro* evidence for the latter proposal.

The mechanism of the possible antiatherogenic activity of lycopene is likewise unclear. Lycopene's antioxidant activity is a possibility. Lycopene has also been found to inhibit cholesterol synthesis, to inhibit HMG-CoA (hydroxymethylglutaryl coenzyme A) reductase activity and to upregulate LDL receptor activity in macrophages. A small preliminary study in humans, reported an LDL-cholesterol-lowering effect of lycopene.

## PHARMACOKINETICS

Lycopene is available in nutritional supplements in the form of an oleoresin, in phospholipid complexes and in oils. In foods, lycopene exists as part of a matrix (in chloroplasts or chromoplasts) within the vegetables or fruit. The efficiency of absorption of lycopene from supplements and foods is variable. The efficiency of absorption of lycopene from tomatoes, in which lycopene is tightly bound within the matrix, is low. It is much higher in processed tomato products. The improved availability of lycopene from processed foods is due to its release from the ruptured plant cells following the mechanical and thermal processing, as well as heat induced-*trans* to *cis* isomerization. *Cis*-lycopene is reported to be more bioavailable than *trans*-lycopene. Lipids increase the absorption of lycopene. For example, the combination of tomato sauce and olive oil delivers more absorbable lycopene than tomato sauce without oil.

Lycopene from supplements or from the matrices of foods is either solubilized in the lipid core of micelles (formed from bile salts and dietary fat) in the lumen of the small intestine or forms clathrate complexes with conjugated bile salts. Micelles and clathrate complexes deliver lycopene to the enterocytes.

Lycopene is released from the enterocytes into the lymphatics in the form of chylomicrons. Lycopene is transported by the lymphatics to the general circulation via the thoracic duct. In the circulation, lipoprotein lipase hydrolyzes much of the triglycerides in the chylomicrons, resulting in the formation of chylomicron remnants. Chylomicron remnants retain apolipoproteins E and B48 on their surfaces and are mainly taken up by hepatocytes and to lesser degrees by other tissues. Within hepatocytes, lycopene is incorporated into lipoproteins. Lycopene is released into the blood from the hepatocytes in the form of very-low density lipoproteins (VLDL) and low-density lipoproteins (LDL). In the

plasma, VLDL is converted by lipoprotein lipase to LDL. Lycopene is transported in the plasma predominantly in the form of LDL.

There is much unknown about the pharmacokinetics of lycopene, in particular its distribution and its metabolism.

## **INDICATIONS AND USAGE**

Lycopene may be helpful in preventing and possibly also managing some cancers, particularly prostate cancer, and may confer some protection against cardiovascular disease. Research, though suggestive of these positive effects, is far from conclusive. And there is far too little evidence of efficacy from very preliminary studies to support any indication for lycopene in the management of HIV disease or other immune dysfunction or in the management of neurodegenerative disorders.

## **RESEARCH SUMMARY**

In a prospective study that followed the eating habits of 47,000 men for six years, a positive correlation was found between tomato-based food consumption and apparent resistance to development of prostate cancer. There was a 35% reduction in risk of developing prostate cancer among those who consumed more than 10 servings of tomato products weekly, compared with those who consumed fewer than 1.5 servings weekly. Most of these servings (82%) were in the form of tomatoes, tomato sauce and pizza. Tomato sauce appeared to be the most protective.

This study reinforced the findings of an earlier prospective study that examined the eating habits of Seventh Day Adventist men over a six-year period. This study found that the relative risk of prostate cancer was 0.60 among Adventist men who ate tomatoes more than five times weekly, compared with those who consumed them less than once weekly.

A recent review of 72 studies found 57 reports of inverse associations between tomato consumption or blood lycopene levels and risk of various types of cancer; 35 of these associations were significant. Evidence of lycopene protective effects were highest for cancers of the prostate, lung and stomach.

While cautioning that these associations do not establish a cause-and-effect relationship, the reviewer observed that "the consistency of the results across numerous studies in diverse populations, for case-control and prospective studies, and for dietary-based and blood-based investigations argues against bias or confounding as the explanation for these findings."

Recently, more direct, though still preliminary, evidence emerged suggestive of

lycopene protective and, perhaps, interventive effects in prostate cancer. In this study, 33 men scheduled for surgery to remove cancerous prostate glands, were randomized to receive 30 milligrams of lycopene (in two 15-milligram capsules) daily or nothing. Dosing commenced 30 days prior to surgery.

Examination of the prostate glands post-surgery revealed that cancer had spread to the very edge of the glands in seven of the 21 lycopene-treated subjects compared with the same extent of spread in 9 of the 12 subjects who did not receive lycopene. Pre-cancerous tissue in the lycopene group was judged to be less abnormal than pre-cancerous tissue in the group that did not receive lycopene. Prostate specific antigen (PSA) fell 20% in the lycopene group between initial dosing and surgery. PSA levels were unchanged in the group not receiving lycopene. Research is ongoing.

Recent epidemiological studies have reported an inverse relationship between higher tissue and serum levels of lycopene and the risk of coronary artery disease. And a recent study in which 19 healthy subjects consumed a variety of tomato products for three weeks reported no change in serum cholesterol levels but significant decrease in lipid peroxidation and LDL-cholesterol oxidation. Numerous *in vitro* and animal studies have also reported results suggestive of lycopene effects that might help prevent or ameliorate cardiovascular disease. Research continues.

## **CONTRINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**

### **CONTRAINDICATIONS**

Lycopene is contraindicated in those hypersensitive to any component of a lycopene-containing product.

### **PRECAUTIONS**

Pregnant women and nursing mothers should obtain their lycopene intake from food sources rather than supplements.

## **INTERACTIONS**

### **DRUGS**

*Cholestyramine:* Concomitant intake of cholestyramine and lycopene may decrease the absorption of lycopene.

*Colestipol:* Concomitant intake of colestipol and lycopene may decrease the

absorption of lycopene.

*Mineral oil:* Concomitant intake of mineral oil and lycopene may reduce the absorption of lycopene.

*Orlistat:* Orlistat may decrease the absorption of lycopene.

## **NUTRITIONAL SUPPLEMENTS**

*Beta-carotene:* Concomitant intake of beta-carotene and lycopene may increase the absorption of lycopene.

*Medium-chain triglycerides:* Concomitant intake of medium-chain triglycerides and lycopene may enhance the absorption of lycopene.

*Pectin:* Concomitant intake of pectin and lycopene may decrease the absorption of lycopene.

## **FOODS**

*Oils:* Dietary oils, such as olive oil, may enhance the absorption of lycopene.

*Olestra:* Olestra may reduce the absorption of lycopene.

## **DOSAGE AND ADMINISTRATION**

Lycopene supplements are available as oleoresin preparations, phospholipid preparations and in oils, such as medium chain triglycerides. Doses range from 5 to 15 milligrams daily.

The optimal dose of lycopene is not known.

The following lists the lycopene contents of some foods:

Food	Lycopene content (micrograms/gram wet weight)
Fresh tomatoes	8.8-42.0
Cooked tomatoes	37
Tomato sauce	62
Tomato paste	54-1,500
Tomato powder	1,126-1,265
Tomato soup (condensed)	80
Tomato juice	50-116

Pizza sauce	127
Ketchup	99-134
Watermelon	23-72
Pink guava	54
Pink grapefruit	34
Papaya	20-53

## HOW SUPPLIED

*Capsules* — 5 mg, 6 mg, 10 mg

*Tablets* — 10 mg

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Participants received various antioxidants far above the RDA, while one group received only placebo. Those participants treated with antioxidants reduced the incidence of developing advanced macular degeneration by approximately 25% compared to placebo. 10/2001

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BETA-CAROTENE

VITAMIN C, VITAMIN E, ZINC 45MG, SELENIUM,

BILBERRY EXTRACT 480-600MG OF 25% ANTHOCYANOSIDES

LYCOPENE

LUTIEN 6-10MG (THEY HAVE 10MG), ZEAXANTHIN (THEY HAVE 500MCG – FROM 200MG STANDARDIZED 5% FLORAGLO LUTIEN EXTRACT – MARIGOLD FLOWER)

GINKGO BILOBA 120-240MG OF 24% GINKO FLAVONS GLYCOSIDE PLUS 6% TERPENE LACTONE

**ALL THE SAME EXCEPT WHAT IS IN RED ABOVE BUT THOSE STUDIES WERE ONLY 8-12 WEEKS LONG**