

Courtesy of American Longevity.

Glade Report for Lycopene, Tomatoes, Tomato-Based Food Products and the Prevention of Cancer

Based on my review of the reliable and credible scientific literature regarding the effects of tomato and tomato-based food product consumption and of dietary supplementation with lycopene on various cancers, I conclude that there is significant scientific agreement in support of the following health claims :

- Lycopene may reduce the risk of cancer.
- Lycopene may reduce the risk of prostate cancer.
- Lycopene may reduce the risk of lung cancer.
- Lycopene may reduce the risk of gastric cancer.
- Lycopene may reduce the risk of colorectal cancer.
- Lycopene may reduce the risk of breast cancer.
- Lycopene may reduce the risk of cervical cancer.
- Lycopene may reduce the risk of endometrial cancer.
- Lycopene may reduce the risk of ovarian cancer.
- Lycopene may reduce the risk of pancreatic cancer.
- Tomatoes may reduce the risk of cancer.
- Tomatoes may reduce the risk of prostate cancer.
- Tomatoes may reduce the risk of lung cancer.
- Tomatoes may reduce the risk of gastric cancer.
- Tomatoes may reduce the risk of colorectal cancer.
- Tomatoes may reduce the risk of breast cancer.
- Tomatoes may reduce the risk of cervical cancer.
- Tomatoes may reduce the risk of endometrial cancer.
- Tomatoes may reduce the risk of ovarian cancer.
- Tomatoes may reduce the risk of pancreatic cancer.
- Lycopene -containing tomato-based foods may reduce the risk of cancer.
- Lycopene -containing tomato-based foods may reduce the risk of prostate cancer.
- Lycopene -containing tomato-based foods may reduce the risk of lung cancer.
- Lycopene -containing tomato-based foods may reduce the risk of gastric cancer.
- Lycopene -containing tomato-based foods may reduce the risk of colorectal cancer.
- Lycopene -containing tomato-based foods may reduce the risk of breast cancer.
- Lycopene -containing tomato-based foods may reduce the risk of cervical cancer.
- Lycopene -containing tomato-based foods may reduce the risk of endometrial cancer.
- Lycopene -containing tomato-based foods may reduce the risk of ovarian cancer.
- Lycopene -containing tomato-based foods may reduce the risk of pancreatic cancer.

I. Lycopene

A. Chemistry

Lycopene (C₄₀ H₅₆) is a natural fat-soluble pigment found in plants where it serves as an accessory light-gathering pigment and free radical quencher. This carotenoid is an open chain polyisoprenoid with 11 conjugated double bonds. Lycopene occurs in food sources predominantly as all- trans -lycopene. Various cis -isomers also are found in human blood and tissues, suggesting post-ingestive isomerization. Because lycopene is acyclic it does not serve as a substrate for β -carotene 15,15'-dioxygenase and therefore cannot be converted to vitamin A. **1-4**

B. Food Sources

The major food sources of lycopene are raw red or pink grapefruit (1419 mcg of lycopene per 100 g edible fruit), raw watermelon (4532 mcg of lycopene per 100 g edible fruit), raw tomatoes (year-round average: 2573 mcg of lycopene per 100 g edible fruit) and processed food products containing tomatoes (tomato juice, 9037 mcg of lycopene per 100 g juice; canned whole tomatoes, 4035 mcg of lycopene per 100 g edible portion; tomato sauce, 15152 mcg of lycopene per 100 g sauce; tomato puree, 21754 to 28764 mcg of lycopene per 100 g puree; tomato paste, 29330 mcg of lycopene per 100 g paste; tomato soup, 14596 mcg of lycopene per 100 g soup; catsup, 17007 mcg of lycopene per 100 g of catsup).

5 Little lycopene is lost during heat processing; for example, the six-fold concentration of tomatoes during the conversion of whole tomatoes into tomato paste is accompanied by a six-fold concentration of lycopene.

6 Similarly, between 90% and 95% of the total lycopene in tomatoes is in the form of trans -lycopene, with the remainder as various cis -isomers; the ratio of trans - to cis -isomers is not affected by the conversion of raw tomatoes into tomato paste. **2,7-10**

Lycopene in foods and food products is extraordinarily stable.

11 Estimates of losses in total lycopene content during the heat processing of tomatoes into tomato juice, paste, soup or sauce have ranged from nil to less than 15%; **9,12-14** Further cooking on a stove for 1 hour did not affect the product's total lycopene content, **12,14** although the ratio of trans - lycopene to cis - lycopene was decreased slightly. **12** Storage of processed tomato juice at 25 o C or 37 o C for 12 months had no effect on total lycopene content, while storage at 4 o C for 12 months reduced total lycopene content by 3%. **12**

C. Bioavailability

Lycopene naturally occurs in plants and is closely associated with the organic matrix of plant cells.

15,16 It appears that lycopene must be released from this matrix in order for absorption to occur.

16,17 This release is effected by gastric acidity **18,19** and by thermal processing of foods containing lycopene prior to their ingestion. **8,11,20** Several investigators have reported that the bioavailability of lycopene (assessed from analysis of acute and subacute changes in post-ingestive circulating total lycopene concentrations) is increased following the conversion of raw tomatoes into juice, paste or puree. **8,20-23** Others have reported that the bioavailability of lycopene in the tomato oleoresin extracts supplied as dietary supplements is greater than is the bioavailability of the lycopene in raw tomatoes but is not different from the bioavailability of lycopene in tomato juice. **24**

Following release from its native organic matrix, or after ingestion as an extract, free lycopene is absorbable only after its incorporation into micelles. **2** Cis -isomers maybe more readily absorbed than trans -isomers (as has been found in ferrets **19**) as a consequence of the greater solubility in mixed micelles of cis -isomers. **2** Any conditions or factors (such as hypochlorhydria, achlorhydria, biliary insufficiency, liver failure, the consumption of a fat-free diet, etc.) that interfere with or reduce postprandial micellar formation will decrease the absorbability of ingested lycopene. **16,25** Conversely, conditions that promote the solubility of lycopene in mixed micelles, such as the presence of monounsaturated fatty acids, will increase the absorbability of ingested lycopene (although low-fat diets appear to have no effect **26,27**). **21,28** Micellar dispersal at the brush border releases lycopene to enter enterocytes via passive diffusion; within enterocytes, lycopene is incorporated into chylomicrons for secretion into the mesenteric lymph system 2 to 6 hours after the consumption of lycopene-containing foods. **2,8** Acting on chylomicrons in the circulation, lipoprotein lipase releases lycopene for uptake by peripheral tissues and organs, including the liver, which repackages lycopene into lipoproteins that are secreted into the circulation 12 to 48 hours later. **8**

In the only study reporting quantitative data on lycopene absorption obtained through the application of compartmental modeling techniques to serum appearance and disappearance data, healthy men were reported to absorb an average of 4.7 mg of total lycopene from daily intakes ranging from 10 to 120 mg. **29** The amount of lycopene absorbed was independent of intake, suggesting the possibility of the potential for saturation of lycopene absorptive mechanisms. Mean efficiencies of absorption of oral lycopene ranged from 34% (10 mg of lycopene consumed) to 5% to 7% (60 mg to 120 mg of lycopene consumed). These estimates of lycopene absorption are greater than that obtained through the use of an in vitro model, which produced an estimate that about 3% of the total lycopene in a stir-fried meal of fresh vegetables was incorporated into micelles (and therefore absorbable), **30** an in vivo model of human micellar formation in situ, which produced an estimate of the efficiency of lycopene absorption of about 2% **31** and an in vivo model of lycopene absorption through association with triglycerides, which resulted in an estimate of the efficiency of lycopene absorption of about 2.5%. **32**

The bioavailabilities of synthetic lycopene preparations have been compared to the bioavailabilities of the lycopene in raw tomatoes and processed tomato products. The bioavailabilities of the synthetic lycopene in microencapsulated beadlets (Lycopene 5% TG, D.S.M. N.V., Heerlen, The Netherlands; LycopVit 10%, BASF, Ludwigshafen, Germany; containing isomeric distributions of lycopene similar to that found in raw tomatoes **23,33**), the extracted "natural source" lycopene in a bead formulation (Lyc-O-Mato™ 6%, LycopRed Natural Products Industries Ltd., Beer-Sheva, Israel) and lycopene in cooked tomato soup have been found to be nearly identical. **23,34** Consistent with the differences in

the bioavailabilities of lycopene in raw and processed tomato-based foods, **8,20-23** the bioavailability of synthetic lycopene has been reported to be significantly greater than the bioavailability of lycopene in unprocessed (raw) tomato juice. **23**

II. The Relationships among the Consumption of Tomatoes and Tomato-Based Foods Containing Lycopene, Dietary Supplementation with Lycopene and Typical Circulating Lycopene Concentrations in Humans

The measured serum or plasma total lycopene concentrations of over 95% of the subjects in a vast array of studies have ranged between 0.1×10^{-6} M and 2×10^{-6} M. **7,10,12,22,29,33-148** These reports are consistent with population survey data that have produced the estimates of serum total lycopene concentrations in the U.S. summarized in Table 1.

Table 1. Serum total lycopene concentrations measured in the National Health and Nutrition Examination Survey III (NHANES III) between 1988 and 1994. **149**

Data from several studies confirm that circulating total lycopene concentrations decline among older adults. **43,121,145** In one study, the mean serum total lycopene concentration of a cohort of men with a mean age of 73 years was only 57% of the mean serum total lycopene concentration of a cohort of men with a mean age of 24 years. **121**

Table 2. Daily lycopene intakes estimated from data obtained in the National Health and Nutrition Examination Survey III (NHANES III) between 1988 and 1994. **154**

Data from the National Health and Nutrition Examination Survey III (NHANES III) indicate that cigarette smokers have significantly lower serum total lycopene concentrations than do nonsmokers. **150** This conclusion is consistent with data obtained from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. **38**

Less data are available concerning lycopene intake. Several surveys (1986 Continuing Survey of Food Intake by Individuals; **151** 1992 National Health Interview Survey; **152** Nutritional Factors in Eye Disease Study **146**) have suggested that mean daily lycopene intake in the U.S. is between 1.6 and 2.6 mg. **149** However, data obtained from the **83,234** participants in the Nurses' Health Study indicates that those women consumed more lycopene on a routine basis (median intake: 6077 mcg). **153** Data obtained from the participants in the NHANES III study (Table 2) contradict these reports, with mean daily lycopene intakes for adults ranging from 4332 mcg to 12656, and median daily lycopene intakes for adults ranging from 842 mcg to 5211 mcg, depending on sex and age. **154** Interestingly, both mean and median daily lycopene intakes were greater among pregnant and lactating adult women than among nonpregnant and nonlactating premenopausal adult women. However, with the exception of men aged 19 to 30 years, over 25% of the participants in the NHANES III study reported no consumption of lycopene-containing foods (and between 10% and 25% of men aged 19 to 30 years reported no consumption of lycopene-containing foods).

Daily lycopene intakes estimated from USDA nutrient composition **5** and food consumption data **155** suggest that lycopene intakes may well average 3- to 10-fold higher than is indicated by other estimates. According to USDA data, per capita consumption of fresh tomatoes averaged 23.3 g daily in 2002 (providing about 0.6 mg of lycopene daily) and is forecast to average 23.7 g daily in 2003 (providing about 0.6 mg of lycopene daily). The consumption of all other tomato-containing foods averaged 87.8 g daily in 2002 (equivalent to 0.7 tomatoes daily **5**) providing between 9 and 27 mg of lycopene daily, depending upon the specific foods and food products consumed) and is forecast to average 89.4 mg daily in 2003 (providing between 9 and 27 mg of lycopene daily, depending upon the specific foods and food products consumed). These data indicate that total daily lycopene consumption averaged between 9 and 28 mg daily in the U.S. in 2002 and 2003. According to these same USDA data, the consumption of tomatoes, tomato-containing foods and food products and lycopene have not changed since 1990.

Data from the **38,445** women participating in the Women's Health Study indicate that lycopene intake is determined primarily by the consumption of tomatoes and tomato-based food products. **156** Among 946 women participating in the Women's Health Initiative, serum total lycopene concentration was independently significantly correlated with the consumption of fresh tomatoes, cooked tomatoes, tomato juice, tomato sauce and tomato salsa. **43** The results of several human studies have

demonstrated that serum or plasma total lycopene concentration is significantly correlated with lycopene intake in healthy men and women **43,65,68,141,144,146** and is unvarying within individuals over a number of years (probably reflecting the relative stability of adult dietary habits). **60,66,77,92,98,111** Therefore, it has been asserted that the measurement of circulating total lycopene concentration in single blood samples provides predictors of long-term lycopene intakes that are sufficiently valid for epidemiologic studies. **111**

In contrast, intentional reduction in lycopene intake produces a significant decrease in circulating lycopene concentrations. **124,125,157** Furthermore, increasing lycopene intake has produced significant increases in serum or plasma total lycopene concentrations in healthy men and women. **12,22,24,34,77-79,85,89,124-126,138** Similarly, increased consumption of tomatoes and tomato-containing foods and food products significantly increased serum or plasma total lycopene concentrations in healthy men and women **23,24,36,43,47,51,69,70,78,79,85,89,91,109,110,122-125,130,134,158** as well as in women with breast cancer, **66,92** men and women with colorectal adenomas, **98** men with prostate cancer, **105** men and women with diabetes, **136** male and female renal transplant recipients, **100** male and female cancer survivors **63** and lactating women. **38**

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