

## Biochemistry of Lycopene

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**Abstract:** Lycopene is a carotenoid found in foods such as tomatoes, tomato products, watermelon, pink grapefruit and guava. Lycopene provides health benefits by being absorbed into body tissues and mounting a defense against damaging free radicals that if left unchecked, create oxidative damage to cells. This leads to conditions such as cancer, heart disease, macular degeneration, diabetes, joint deterioration and accelerated aging. The body obtains antioxidants from many of the foods that comprise a healthy diet however many people fail to eat enough of these recommended foods. In addition, the city environments are overloaded with extra free radicals courtesy of sources like industrial pollution, motor vehicles and smoking. Hence, there is a need to increase the dietary intake of an effective antioxidant such as lycopene. All antioxidants have shown a role in destroying free radicals and thereby reducing the damage to all cells in the body. Lycopene inhibits free radical damage to LDL cholesterol with its antioxidant action preventing oxidation to LDL cholesterol. Oxidation of cholesterol is a process that can cause a great deal of cell damage. Lycopene boosts the body's natural antioxidant defences and protects against DNA damage thus promotes heart health. Numerous epidemiological studies have linked diets that are high in lycopene intake with a reduced risk of cancer and degenerative diseases. This study summarizes the information about lycopene and presents the current knowledge with respect to its role in human health and disease.

**Key words:** Antioxidant, free radicals, lycopene, dietary sources, tomato, product

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### INTRODUCTION

Lycopene is a pigment that gives fruits and vegetables such as tomatoes, pink grapefruit and watermelon their red color. It also appears to have strong antioxidant capabilities. Lycopene is one of the carotenes and a member of the carotenoid family. The lycopene antioxidant is described as one of the most active antioxidants of all the carotenoid pigments (Miller *et al.*, 1996). It is also the most common carotenoid found in the human body.

Most people have much higher levels of lycopene than  $\beta$ -carotene in their liver, adrenal glands, lungs, prostate, colon and skin which is not such a bad thing, considering it has twice the antioxidant power of  $\beta$ -carotene (Kaplan *et al.*, 1990). Lycopene is a phytochemical, synthesized by plants and microorganisms but not by animals. It is an acyclic isomer of  $\beta$ -carotene and has no vitamin A activity (Rao and Agarwal, 1999). This highly unsaturated hydrocarbon contains 11 conjugated and 2 unconjugated double bonds making it longer than any other carotenoid (Nguyen and Schwartz, 1999).

**Squalene:** An example of a compound with tail-to-tail bonding of two sesquiterpene units. The dashed line indicates the bonding location (Johnson *et al.*, 1997).

As a polyene, it undergoes cis-trans isomerization induced by light, thermal energy and chemical reactions. Lycopene obtained from plants tends to exist in an all-trans configuration, the most thermodynamically stable form. Humans cannot produce lycopene and must ingest fruits, absorb the lycopene and process it for use in the body. In human plasma, lycopene is present as an isomeric mixture with 50% as cis isomers (Clinton *et al.*, 1996). As an antioxidant, lycopene has a singlet-oxygen-quenching ability twice as high as that of  $\beta$ -carotene (vitamin A relative) and 10 times higher than that of  $\alpha$ -tocopherol (vitamin E relative). One non-oxidative activity is the regulation of gap-junction communication between cells (Johnson *et al.*, 1997). The body does not produce lycopene so you must eat foods rich in lycopene to benefit from its considerable antioxidant powers. However, cooking fresh tomatoes with a little oil greatly increases lycopene absorption and other fresh fruits and vegetables such as watermelon, pink grapefruit and red peppers also contain lycopene (Nguyen and Schwartz, 1997).

Many fruits and vegetables contain lycopene. However, the richer sources include dried apricots, pink

grapefruit, pink guava, anything containing tomato sauce and watermelon. Fruits and vegetables that are high in lycopene include gac, tomatoes, watermelon, pink grapefruit, pink guava, papaya, seabuckthorn, wolfberry and rosehip (Clinton *et al.*, 1996). Fatty acids and carotenoid composition in gac (*Momordica cochinchinensis* Spreng) mean that it has the highest content of lycopene of any known fruit or vegetable >70 times more than tomatoes for example (Ishida *et al.*, 2004). However, due to gac's rarity outside its native region of Southeast Asia, tomatoes and tomato-based sauces, juices and ketchup account for >85% of the dietary intake of lycopene for most people (Rao and Rao, 2007). Unlike other fruits and vegetables where nutritional content such as vitamin C is diminished upon cooking, processing of tomatoes increases the concentration of bioavailable lycopene. Lycopene is also found to concentrate in the adrenal, liver, testes and prostate. However, unlike other carotenoids (Lycopene Ishida *et al.*, 2004). Lycopene levels in serum or tissues do not correlate well with overall intake of fruits and vegetables. Lycopene is insoluble in water and can be dissolved only in organic solvents and oil (Nguyen and Schwartz, 1997). Because of its non-polarity, lycopene in food preparation will stain any sufficiently porous material including most plastics (Johnson *et al.*, 1997). While a tomato stain can be fairly easily removed from fabric (provided the stain is fresh), lycopene diffuses into plastic making it impossible to remove with hot water or detergent. If lycopene is oxidized (for example by reacting with bleaches or acids), the double bonds between the carbon atoms will be broken. Lycopene's configuration enables it to inactivate free radicals. Because free radicals are electrochemically imbalanced molecules they are highly aggressive, ready to react with cell components and cause permanent damage. Oxygen-derived free radicals are the most reactive species. These toxic chemicals are formed naturally as by-products during oxidative cellular metabolism. As an antioxidant, lycopene has a singlet-oxygen-quenching ability twice as high as that of  $\beta$ -carotene (vitamin A relative) and 10 times higher than that of  $\alpha$ -tocopherol (vitamin E relative). One non-oxidative activity is the regulation of gap-junction communication between cells. Lycopene participates in a host of chemical reactions hypothesized to prevent carcinogenesis and atherogenesis by protecting critical cellular biomolecules, including lipids, proteins and DNA (Rao and Agarwal, 1998; Pool-Zobel *et al.*, 1997).

Lycopene and other carotenoids are found to concentrate in low-density and very-low-density lipoprotein fractions of the serum (Clinton, 1998). Tomatoes are a potent source of lycopene but tomatoes

are also an excellent source of flavonoids and polyphenols which are associated with lower risk of cancer. In addition, tomatoes contain significant amounts of vitamin C, potassium as well as some vitamin A and E (Campbell *et al.*, 2004). There were no protective effects of raw tomatoes, cooked tomatoes or estimated lycopene intake. However both total vegetable intake and cruciferous vegetable intake were significantly protective (Cohen *et al.*, 2000).

## RESULTS AND DISCUSSION

Antioxidants are protective agents that inactivate reactive oxygen species and therefore significantly delay or prevent oxidative damage. Antioxidants such as superoxide dismutase, catalase and glutathione peroxidase are naturally present within human cells. In addition, antioxidants such as vitamin E, C, polyphenols and carotenoids are available from food. Current dietary guidelines to combat chronic diseases including cancer and coronary artery disease recommend increased intake of plant foods including fruits and vegetables which are rich sources of antioxidants (Agarwal and Rao, 1998). The role of dietary antioxidants including vitamin C, E, carotenoids and polyphenols in disease prevention has received much attention in recent years (Halliwell *et al.*, 1995). Antioxidant properties of lycopene are well documented. It has both oxidative and non-oxidative properties that help in its cancer-fighting properties (Block, 1992; Rimm *et al.*, 1993; Giovannucci *et al.*, 1995; Steinmetz and Potter, 1996).

Lycopene has attracted a lot of attention since 1995, when a 6 year study by Harvard University of nearly 48,000 men found that those who ate at least 10 servings of food containing tomato sauce or tomatoes per week were 45% less likely to develop prostate cancer. The study also found that those who ate 4-7 servings per week were 20% less likely to develop it (Sesso *et al.*, 2003). Researchers have also found that lycopene may help reduce the risk of heart disease. One study found that women who ate at least seven servings a week of tomato-based products had a 30% reduced risk of cardiovascular disease (Di Mascio *et al.*, 1989).

Lycopene, due to lack of a beta ionone ring structure cannot form vitamin A. It also inactivates free radicals; these free radicals have a special property of reacting with body cells. These free radicals in turn create cell damage, especially radicals generated from oxygen which are the most damaging. The effectiveness of lycopene as an antioxidant can be proved by comparing it with other antioxidants. It has twice the ability of  $\beta$ -carotene and 10 times more than  $\alpha$ -tocopherol. It also reduces LDL

oxidation and helps in reducing levels of blood cholesterol. Some more benefits of lycopene are reducing macular degenerative disease and cancers of the lung as well as the cervix. Giovannucci recently reviewed 72 epidemiological studies including ecological, case-control, dietary and blood-specimen-based investigations of tomatoes, tomato-based products, lycopene and cancer. In 57 studies, there was an inverse association between tomato intake or circulating lycopene levels and the risk of several types of cancer in 35 cases the association was statistically significant. None of the studies showed adverse effects of high tomato intake or high lycopene levels. Lycopene may be the most powerful carotenoid quencher of singlet oxygen (Berneburg *et al.*, 1999). Singlet oxygen produced during exposure to ultraviolet light is a primary cause of skin aging (Giovannucci *et al.*, 1995).

Given its antioxidant properties, substantial scientific and clinical research has been devoted to a possible correlation between lycopene consumption and general health. Early research suggested some amelioration of cardiovascular disease, cancer, diabetes, osteoporosis and even male infertility (Levy *et al.*, 1995). There have been several studies produced that analyzed the anti-cancer properties of lycopene, although research has been primarily inconclusive. Evidence for lycopene's benefit was strongest for cancers of the lung, stomach and prostate gland. Lycopene is not modified by vitamin A in the body so it can be accessible for other benefits such as antioxidation. The absence of the beta-ionone ring structure for lycopene increases its antioxidant action. Lycopene is also the most efficient oxygen and free radical quencher and is the prime carotenoid in plasma and other tissues. Lycopene is also found in lung tissue and is valuable in protecting lymphocytes from NO<sub>2</sub> damage found in lung cancer. Lycopene may also help decrease the impact of oxidative load from pylori infections in the stomach. The tomato-derived carotenoid lycopene may reduce the risk of cancer by activating special cancer-preventive enzymes such as phase II detoxification enzymes which remove harmful carcinogens from cells and the body (Sesso *et al.*, 2003). In one study of lycopene as a inhibitor of human cancer cell proliferation, it was found that unlike cancer cells, human fibroblasts were less sensitive to lycopene and the cells gradually escaped growth inhibition over time. In addition to its inhibitory effect on basal endometrial cancer cell proliferation, lycopene was also found to suppress insulin-like growth factor-I-stimulated growth. Insulin-like growth factors are major autocrine/paracrine regulators of mammary and endometrial cancer cell growth. Therefore, lycopene interference in this major autocrine/paracrine

system may open new avenues for research on the role of lycopene in the regulation of endometrial cancer and other tumors (Pollack *et al.*, 1997). In different studies however lycopene was even found to have an inhibitory effect on cataract development (Nahum *et al.*, 2001) and several different kinds of cancer cells including breast and endometrial cancer cells (Narisawa *et al.*, 1996) and colon cancer cells (Cohen *et al.*, 2000; Johnson *et al.*, 1997). After extensive review reported in November 2005, the United States Food and Drug Administration has cast significant doubt on the potential for lowering the risk of disease showing no link between lycopene and the prevention of prostate cancer although, it is suggested that eating whole tomatoes does provide benefit, perhaps because as yet undiscovered compounds (other than lycopene) are the beneficial agents.

Cohen *et al.* (2000) and Giovannucci (1999) completed a nested case-control study in King Country Washington with 628 patients and 602 control patients. Food-frequency questionnaires were completed and total fruit and vegetable intake was summarized. Studies show that lycopene helps prevent prostate, lung and stomach cancers. There is also some evidence that cancers of the pancreas, colon and rectum, esophagus, oral cavity, breast and cervix could be reduced with increased lycopene intake (Neuman *et al.*, 2000). A few studies have suggested the benefits of lycopene for exercise-induced asthma (Schwarz *et al.*, 2008) and benign prostatic hyperplasia (Etminan *et al.*, 2004). Data from epidemiologic studies indicate an inverse relationship between dietary and supplemental lycopene consumption and the risk of cancer particularly prostate (Giovannucci, 2002) lung and stomach cancers as well as Estrogen Receptor (ER) and Progesterone Receptor (PR) positive breast cancers (Giovannucci *et al.*, 2002).

Besides cardiovascular diseases, recent evidence points to carotenoids as effective antioxidants for inhibiting the development of degenerative diseases such as cancer, cataracts, etc. Intake of  $\beta$ -carotene has been inversely linked to incidence of lung cancer as well as similar correlations between lutein and macular disease and between lycopene or tomato-based products and prostate cancer (Cooper *et al.*, 1999; Block *et al.*, 1992). However, lycopene, being the strongest singlet oxygen quencher as well as a potent antioxidant compared to other carotenoids has rarely been tested in studies for its role in cardiovascular disease prevention. Although, some studies (Franceschi *et al.*, 1998; Suganuma and Inakuma, 1999) reported inverse correlation between incidence for degenerative diseases and the consumption of fruit and vegetables instead of correlations to single ingredients of these foods, there is only scarce scientific knowledge on

the interactions between different food components regarding their protective potential. The oxidation-protecting effect of lycopene and tomatoes has been shown in both human and animal studies (Agarwal and Rao, 1998; Salonen *et al.*, 1992). A reduced oxidative modification of LDL may be one of the mechanisms by which lycopene reduces the risk of CAD and atherosclerotic progression (Salonen *et al.*, 1997). Many researchers have postulated that antioxidants are crucial in preventing cell damage by free radicals and can be useful tools in preventing degenerative diseases associated with aging including heart disease and cancer (Wood *et al.*, 2008).

A study on adult asthma patients showed the intake of tomato juice or a tomato extract (both corresponding to a daily intake of 45 mg lycopene) inverted the unfavorable effect of a low anti-oxidant diet on asthma and airway inflammation. Intake of tomato juice or lycopene extract resulted in a reduced influx of white blood cells in the airway. Treatment with the lycopene extract also reduced the activity of neutrophil elastase, a role in degenerative and inflammatory diseases (Franceschi *et al.*, 1994). High intake of tomatoes was consistently associated with a reduced risk of digestive tract cancers (especially stomach, colon and rectal) in a case control study from Italy where the cases were patients with histologically-confirmed cancers of oral cavity, pharynx, esophagus, stomach, colon and rectum and the controls were patients with unrelated conditions (Sharma *et al.*, 2003). Epidemiological investigations to study the role of lycopene in relation to chronic diseases has focused primarily on cancers. This might be explained by the fact that lycopene is an antioxidant that reduces oxidative stress which plays a major role in numerous health concerns for women including breast cancer, cervical cancer, cardiovascular disease and preeclampsia (Sharma *et al.*, 2003). Conflicting evidence has emerged regarding the association between lycopene and lung cancer. One study explained in a 2009 American Journal of Epidemiology article found that lycopene supplementation did not lead to an increased risk of getting lung cancer.

## CONCLUSION

The benefits of tomatoes and tomato products are often attributed to the carotenoid lycopene. However a direct benefit of lycopene has not been proven and other compounds in tomatoes alone or interacting with lycopene may be important. It is critical to recognize that the current evidence regarding dietary intake and lycopene blood concentrations reflects consumption of

tomatoes and tomato products rather than purified lycopene supplements. Nutrition is a very important factor in the development of our understanding of cancer. A team of scientists found plants work harder on the ingredients which were made. By various mechanisms of phytochemicals cancer cells are known to be neutralized. As a result, researchers must attach importance to nutritional consciousness. Lycopene is a powerful antioxidant with numerous useful functions to the experimental research which supports that an awareness of food stuffs containing lycopene is important for our future and the health. Lycopene is nontoxic and is commonly found in the diet but cases of excessive carotenoid intake have been reported. Lycopene in organic fruits and vegetables is important for the health. Dietary intakes of tomatoes and tomato products containing lycopene have been shown to be associated with a decreased risk of chronic diseases such as cancer and cardiovascular diseases in several recent studies. Serum and tissue lycopene levels have also been inversely related with the risk of chronic disease. These findings add further support to current dietary recommendations to increase the consumption of fruits and vegetables to reduce the risk of cancer. This review summarizes information about lycopene and presents the most current knowledge with respect to its role in disease and human health.

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