Chapter 5
Lycopene Bioavailability and Its Effects on Health

Ana Lucia A. Ferreira and Camila Renata Corrêa

Abstract Lycopene is a lipophilic carotenoid which is responsible for the red color in various fruits and vegetables and is commonly found in tomatoes. Lycopene is one of the most potent antioxidants among the dietary carotenoids mainly due to its many conjugated double bounds, and it also has the strongest singlet oxygen-quenching ability compared to other carotenoids. Besides acting as antioxidant, other mechanisms such as immune system stimulation, cell cycle regulations, gap junction communication enhancement, mutagenesis reduction, tumor cell proliferation inhibition, antitumor immune response improvement, and anti-inflammatory action have also been identified with this carotenoid. Lycopene, as a dietary source of a carotenoid, has received considerable scientific interest in several chronic diseases including cancer, cardiovascular diseases, osteoporosis, and diabetes. It is one of the major carotenoid in the diet of North Americans and Europeans. Besides tomato, lycopene is found in watermelon, guava, papaya, and apricot. The amount of lycopene in fruits and vegetables varies according to the season, stage of ripeness, variety, geographical and climatic effect, planting location, and postharvest handling and storage; in general, the more reddish the food, the greater the concentration of lycopene. The highest concentrations of lycopene are generally in the bark of food sources as compared to the pulp. Its largest concentration is found in food produced in regions with warm climates. Several factors affect the bioavailability of lycopene, such as the food processing. Ingestion of cooked tomato in oil medium increased human serum lycopene levels than consumption of unprocessed tomato juice.

Keywords Lycopene • Bioavailability • Tomato • Oxidative stress

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Table 5.1 Lycopene content of fruits and vegetables

Food	State	Concentration (μg/100 g wet weight)	References
Tomatoes	Fresh raw	2,937	Scott and Hart (1995)
Tomatoes	Fresh, cooked	3,703	Scott and Hart (1995)
Tomatoes	Sauce canned	6,205	Scott and Hart (1995)
Tomato	Concentrated canned sauce	6,500	Mangels et al. (1993)
Tomato	Fresh raw	3,100	Mangels et al. (1993)
Tomato	Canned juice	8,580	Mangels et al. (1993)
Tomato	Ketchup	9,900	Mangels et al. (1993)
Apricot	Dehydrated	864	Mangels et al. (1993)
Apricot	Canned	65	Mangels et al. (1993)
Apricot	Raw	5	Mangels et al. (1993)
Guava	Juice	3,340	Mangels et al. (1993)
Guava	Raw	5,400	Mangels et al. (1993)
Watermelon	Fresh raw	4,100	Mangels et al. (1993)
Papaya	Fresh	2,000–5,300	Ong and Tee (1992)

5.1 Introduction

Lycopene is a carotenoid that gives red color to many fruits such as tomatoes, guava, and watermelon among other foods. The lycopene amount in fruits and vegetables varies according to the season, stage of ripeness, variety, geographical and climatic effect, planting location, and postharvest handling and storage. In general, the more reddish the food is, the greater the concentration of lycopene (Table 5.1). The highest concentrations of lycopene are generally in the bark of food as compared to the pulp, and its largest concentration is found in foods produced in hot climate regions (Moritz and Tramonte 2006).

Tomato is the most abundant source of lycopene. The consumption of tomatoes has not been reported in Europe and USA until the sixteenth and eighteenth centuries, respectively. However, before the sixteenth century, the tomato was originated in Peru and Ecuador, where it was introduced and cultivated as food by the Incas. Around 1529, the Aztec emperor Montezuma offered tomatoes as a gift to a Spanish conquistador, Hernando Cortés. This act was probably responsible for the introduction of lycopene in the USA (Texas, Arizona and California), Mexico, and Europe (Gerster 1997).

Lycopene is a natural pigment synthesized by plants and microorganisms to absorb light during photosynthesis (Moritz and Tramonte 2006). It is an unsaturated symmetrical and acyclic hydrocarbon with a molecular formula of $C_{40}H_{56}$ and a molecular weight is 536.85 daltons. It occurs naturally as all *trans* form and its chain containing 13 double bonds of which 11 are conjugated (Fig. 5.1). It may undergo isomerization (Fig. 5.2) from *trans*- to mono-*cis* or poly-*cis* when exposed to high temperatures, light, oxygen, acids, and metal ions. The *trans* form

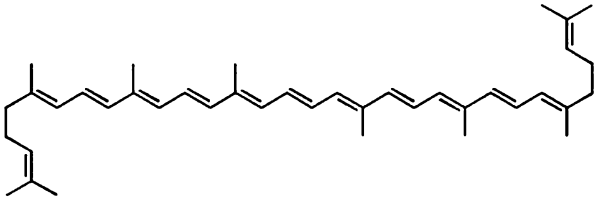

Fig. 5.1 Chemical structure of lycopene

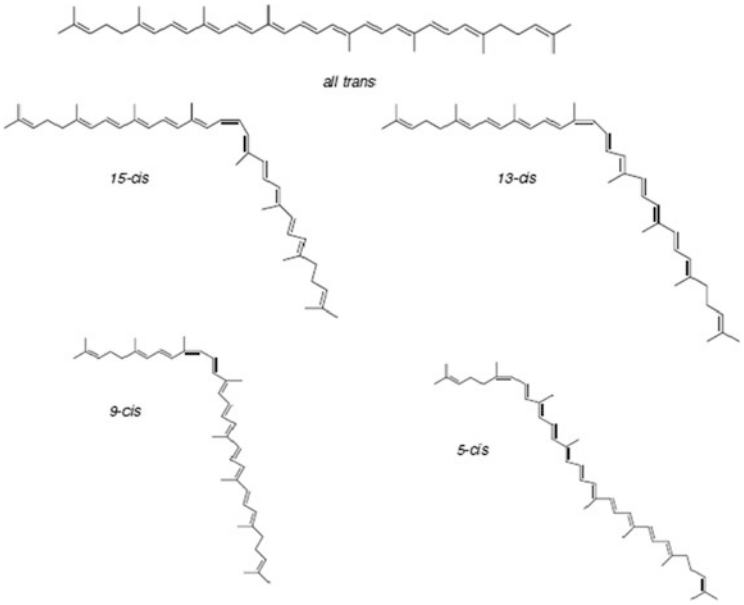

Fig. 5.2 Structures of *cis* and *trans* isomers of lycopene

is considered to be more stable and is the most common form present in foods (Rao et al. 2006).

Lycopene is a lipophilic compound with hydrophobic characteristics due to its acyclic structure and 11 linear conjugated double bonds that make it more soluble in organic solvents such as acetone, chloroform, hexane, benzene, methylene chloride, and petroleum ether (Agarwal and Rao 2000). This system of conjugated double bonds is a chromophore responsible for its ability to absorb light in the visible range, consequently by its coloring power, being responsible for the orange-red coloration of plants. At least seven conjugated double bonds are necessary for a carotenoid to be colored. When the conjugated system is extended, the color is also intensified (Rodriguez-Amaya 2002; Niizu 2003).

To be absorbed by the body, lycopene needs to be released from food, solubilized in the intestine in the presence of fat and bile acids, and incorporated into

dietary lipid micelles. It is absorbed by passive diffusion through the intestinal mucosa cell. After its uptake by cells of the small intestine, lycopene is rather carried in the plasma by low density lipoprotein (LDL) (60 %), HDL (25 %), and VLDL (15 %) (Parker 1989). It is stored in sites rich in LDL receptors (liver, testis, prostate, ovary, adrenal, and adipose tissue). The excretion of this carotenoid is performed mainly via fecal. Twelve to 33 days is the estimate period to eliminate the lycopene ingested (Rock et al. 1992).

Lycopene is present in plasma (~0.5 μmol/L) and varying amounts in human tissues. Adrenals and testes have higher concentrations of lycopene (~20 nmol/g wet tissue) (Stahl and Sies 1996). In fact, study of plasma samples and tissue obtained at autopsy showed that the highest levels of lycopene were found in the testes, adrenal glands, and liver. Brain showed carotenoid concentration below the levels of detection by HPLC (Stahl et al. 1992; Kaplan et al. 1990). Samples of human prostates obtained by prostatectomy showed 0.6 and 0.9 nmol of lycopene per g wet tissue regions in malignant and benign prostate, respectively (Kaplan et al. 1990). The authors speculated that the reason for this difference is due to the fact that tissue derived from normal prostate is metabolically less active than in cancerous tissue in uptake carotenoids from plasma (Clinton et al. 1996). A cross-sectional study examined healthy adult (12 women and 13 men) by dietary carotenoid intake, serum, and adipose tissue biopsies (abdomen, buttock, inner thigh). The carotenoid with the highest median concentration in adipose tissue was *cis*-lycopene, regardless of whether the adipose tissue was taken from the thigh, buttocks, or abdomen. Lycopene median serum concentration was 405.8 nmol/L (*trans*- + *cis*-). Moreover, serum concentrations of *trans*-lycopene were significantly correlated with their levels in buttock adipose tissue ($p < 0.02$) (Epstein et al. 2009).

Although lycopene lacks provitamin A activity, this carotenoid has attracted attention in part due its antioxidant properties (Clinton 1998; Stahl and Sies 1996; Gerster 1997; Giovannucci 1999; Rao and Agarwal 2000) by protecting against oxidative damage implicated in the pathogenesis of several human chronic diseases. However, other mechanisms such as immune system stimulation, cell cycle regulations (Rao et al. 2006), gap junction communication enhancement (i.e., increasing cell–cell communication) (Clinton 1998; Zhang et al. 1991), mutagenesis reduction, tumor cell proliferation inhibition, antitumor immune response improvement (Zhang et al. 1991), and anti-inflammatory action (Luvizotto et al. 2013; Marcotorchino et al. 2012; Bignotto et al. 2009) have also been identified.

Lycopene is one of the most potent antioxidants among the dietary carotenoids mainly due to its many conjugated double bounds (Stahl and Sies 1993), and it also has the strongest singlet oxygen-quenching ability compared to other carotenoids (Di Mascio et al. 1989). This singlet oxygen-quenching ability of lycopene is twice as high as that of β-carotene and ten times higher than of α-tocopherol (Agarwal and Rao 2000). Besides quenching singlet molecular oxygen and peroxyl radicals (Stahl and Sies 2003), strong interaction of lycopene has been shown to occur with other ROS such as H_2O_2 (Wang et al. 2004), which can generate the hydroxyl radical, known to induce membrane lipid peroxidation and DNA strand scission (Lu et al. 1995).

The toxicity of lycopene is minimal. The toxicity (as irritation reactions only) in skin and eyes was identified in Sprague-Dawley when lycopene dose was higher

than 5,000 mg/kg body wt/day. The tolerable intake (45 mg/kg body wt/day) for humans was calculated using the value of 10 as a safety factor for intraspecies differences and factor 10 for interspecies difference. Therefore, the lethal dose (LD_{50}) for humans is 45 mg/kg/day of lycopene (Matulka et al. 2004).

5.2 Bioavailability

Lycopene is not synthesized by body and therefore its levels in plasma and human tissues reflect the dietary intake. Factors that influence the bioavailability of lycopene are its release from the food matrix due to processing, presence of dietary lipids, and heat-induced isomerization from the all-*trans* to *cis* form. They all enhance lycopene absorption into the body. Other events affect the absorption of dietary lycopene including age, gender, hormonal status, body mass and composition, blood lipid levels, smoking, alcohol, and the presence of other carotenoids in the food (Rao et al. 2006; Khachik et al. 2002; McClain and Bausch 2003; Bramley 2000).

The products derived from tomatoes are the richest source of lycopene. The amount of lycopene is directly related to the ripening of tomato (Pangaribuan and Irving 2006). The absorption of lycopene appears to be higher in baked products using tomatoes and influenced by the amount of dietary fat. Furthermore, some fibers, such as pectin, can reduce the absorption of lycopene due to increased viscosity (Lugasi et al. 2003). During cooking tomato, lycopene losses are minimal. Actually, ingestion of cooked tomato juice in corn oil (1 %) for 1 h enhances significantly (2–3 times) serum lycopene as compared to unprocessed tomato juice (Stahl and Sies 1992).

Current knowledge of the bioavailability of lycopene in humans is limited due to the inability to distinguish newly administered lycopene from the body reserves of lycopene. A quantitative method to assess the absorption and relative bioavailability of newly absorbed synthetic or natural lycopene was developed using two deuterated lycopene sources, in conjunction with an advanced liquid chromatography/atmospheric pressure chemical ionization-mass spectrometry (LC/APCI-MS) to analyze newly absorbed lycopene in blood samples of study subjects. We previously evaluated the bioavailability of lycopene (deuterium-labeled lycopene, $^{2}H_{10}$ lycopene) obtained either from intrinsically labeled tomatoes (steamed and pureed) grown hydroponically (16.3 and 17.4 μmol lycopene) or chemical synthesis (11 μmol lycopene) in humans. Our results showed that the relative bioavailability of synthetic lycopene in oil was three times more bioavailable than that from tomatoes, up to 34 days after taking $^{2}H_{10}$ lycopene dose. It is well known that tomato processing, such as cooking in oil, can increase the absorption and bioavailability of lycopene from tomato. Thus, although our preparation involved steaming the tomatoes for 10 min and giving the dose with a liquid diet containing fat, the tomatoes were not heated with oil, and this might not have been optimal for absorption (Tang et al. 2005).

The structure and physical and chemical properties of lycopene in foods determine their use by organism (Gartner et al. 1997). The bioavailability of lycopene is also related to its isomeric forms. Although lycopene is present in foods, mostly in the form of *trans*- (80–97 %), the *cis*- seems to be better absorbed and found in the human body due to its short length and its better solubility in micelles (Boileau 1999). The acidic pH of the stomach seems to contribute with small part in the conversion from all-*trans* to *cis*-isomers of lycopene. The improved bioavailability of *cis*-isomers was demonstrated in a study by Boileau (1999) who compared the bioavailability of lycopene in different isomeric forms in vivo. It was reported the presence of 52 % *cis* isomers in ferret serum 2 h after the intestine was perfused with lycopene [LycoRed in soybean oil (40 mg/kg body wt)] that contained 91 % all-*trans*-lycopene (Boileau 1999).

We have previously demonstrated (Ferreira et al. 2000) the sample preparation and animal species also can interfere on extraction efficiency of lycopene isomers. Oral treatment with 4.6 mg lycopene/(kg body wt/day) for 9 weeks resulted in the appearance of lycopene in plasma and all tissues studied in both rats and ferrets. Ferret plasma contained 11.2 nmol/L total lycopene, 33 % of which was present as *cis* isomers. With the exception of the rat testes, sample saponification resulted in a higher extraction efficiency of lycopene isomers from the tissues of both animals. All-*trans*-lycopene was the major isomer detected in the rat tissues, except for the prostate, either by saponification or by direct extraction. In marked contrast to rats, ferret tissues had predominantly *cis*-lycopene in most tissues, whereas all-*trans*-lycopene was the major isomer in the prostate and plasma. The study also showed rats absorbed lycopene more effectively than ferrets. Thus, there are species differences in the ability to absorb and store lycopene in vivo and in the ability to absorb and concentrate the various lycopene isomers in specific tissues.

There are also some indications of in vivo *trans* to *cis* isomerization reactions. Very little is known about the in vivo metabolism of lycopene. In 1996, Clinton et al. suggested the occurrence of in vivo isomerization of lycopene, since they detected higher amounts of *cis*-lycopene than all-*trans*-lycopene in human serum and in both benign and malignant prostate tissue (Clinton et al. 1996). Using the post-mitochondrial fraction of rat intestinal mucosa, we have investigated lycopene metabolism (Ferreira et al. 2003). The incubation media was composed of cofactors and lipoxygenase (soybean). The addition of lipoxygenase (LOX) into the incubation significantly increased the production of lycopene metabolites. The enzymatic incubation products of deutered lycopene ($^{2}H_{10}$ lycopene) were separated using high performance liquid chromatography (HPLC) and analyzed by UV/Visible spectrophotometer and LC/APCI-MS spectroscopy. We have identified two types of products: cleavage products and oxidation products. The cleavage products were likely: 3-keto-apo-13-lycopenone (or 6,10,14-trimethyl-12-one-3,5,7,9,13-pentadecapentaen-2-one) and 3,4-dehydro-5,6-dihydro-15,15′-apo-lycopenal (or 3,7,11,15-tetramethyl-2,4,6,8,12,14-hexadecahexaen-1-al). The oxidative metabolites are likely: 2-apo-5,8-lycopenal-furanoxide; lycopene-5, 6, 5′,6′-diepoxide; lycopene-5,8-furanoxide isomer (I); lycopene-5,8-epoxide isomer (II); and 3-keto-lycopene-5′,8′-furanoxide. Our incubation procedure produced significant amount of

cis isomers (peaks lycopene-5,8-furanoxide isomer (I) and lycopene-5,8-epoxide isomer (II)) from the original *all-trans* lycopene. Although the biological importance of these lycopene metabolites, including their *cis–trans* isomers, is still unknown, the health effect attributed to lycopene in humans may be due to the activity of some of these oxidation products (Ferreira et al. 2003). Metabolism of lycopene has also been studied in pathological conditions. We have investigated lycopene metabolism in post-mitochondrial fraction of intestinal mucosa from rats treated with doxorubicin (a chemotherapic agent; multiple doxorubicin doses; cumulative dose, 16 mg/kg body wt). As previously demonstrated (Ferreira et al. 2003), we added LOX to obtain maximum production of the metabolic products. Deuterated lycopene ($^2H_{10}$) was used with a characteristic enrichment profile that helped us to identify the lycopene cleavage products. Lycopene metabolites consisted of both enzyme-catalyzed cleavage products (3-keto-apo-13-lycopene) as well as oxidative products (2-ene-5,8-lycopene-furanoxide, *cis*-2-ene-5,8-lycopene-furanoxide, *cis*-lycopene 1,2,5′,6′-diepoxide, lycopene-5,6,5′,6′-diepoxide, *cis*-lycopene-1,6-epoxide, and lycopene-1,6-epoxide). When compared with our previous study, new oxidative products were found, such as *cis*-lycopene 1,2,5′,6′-diepoxide, *cis*-lycopene-1,6-epoxide, and lycopene-1,6-epoxide. This difference may be due to the different rat strain used. The quantification of these products revealed that, when compared to control group (rats treated with saline), intestinal mucosa from doxorubicin group had significantly higher amounts of intact lycopene and lower oxidative cleavage products, suggesting that doxorubicin may have contributed to preventing the lycopene breakdown process and therefore preserving lycopene in its intact form (Ferreira et al. 2007a). From these data, we cannot suggest that cancer patients under doxorubicin therapy should or not eat tomato products. Our results indicated that doxorubicin seems to retard lycopene metabolism (i.e., preserves $^2H_{10}$ lycopene in its intact form (all-*trans*-) and lowers oxidative cleavage products of $^2H_{10}$ lycopene). Considering that the intact lycopene has higher antioxidant activity as compared to those of its metabolites, and that there is no known toxicity of lycopene, it may be beneficial for cancer patients with doxorubicin therapy (especially in the acute treatment) to consume lycopene-rich foods such as tomatoes or tomatoes products (Ferreira et al. 2007a).

5.3 Amount of Lycopene in Food Sources

The amount of lycopene in fruits and vegetables varies according to the season, stage of ripeness, variety, geographical and climatic effect, planting location, and postharvest handling and storage. In general, the more reddish the food, the greater the concentration of lycopene. The highest concentrations of lycopene are generally in the bark of food sources, when compared to the pulp, and its largest concentration is found in food produced in regions with hot climates (Moritz and Tramonte 2006). Tomato and its derivate products, guava, watermelon, and papaya are the main sources of lycopene (Table 5.1).

Latin America has a wide variety of foods with high concentrations of different carotenoids. Besides tomato, lycopene is the predominant carotenoid in papaya, guava and red cherry. Climatic and geographical differences can interfere in lycopene amount (Rodriguez-Amaya 1999).

The concentration of lycopene of tomato also displays great variation, particularly with regard to color, ripeness, and the planting site climate. It is considered that summer generates fruit with more lycopene content than winter or spring (Stahl and Sies 1993). Studies have shown different results for the same analysis of a variety of tomatoes (*Lycopersicon esculentum*). The colors of tomato species range from yellow to orange-red due to the reason lycopene/fruit carotene. Ripe tomato contains higher amounts of lycopene *trans* beta-carotene (Giovannucci 1999). Several Brazilian vegetables show expressive content of lycopene (μg/g of food), such as canned concentrate tomato (23,500), ripe pitanga (7,600), pink guava (6,900), mamao formosa (2,600), caja pulp (560), bocaiuva (170), and acerola (70–160) (Rodriguez-Amaya 2002).

Thus, we can notice that there are a wide range in concentration, amount, and bioavailability of lycopene in foods. This carotenoid is the one which takes action by itself, not being a precursor of vitamin A. Tomato, tomato-based sauces, and its juices are the most abundant sources of this compound for human (Giovannucci 1999).

High performance liquid chromatography (HPLC) system is considered gold standard for measurement of lycopene concentration in foods, blood, and tissue. One of the most used methods of extraction was described by Riso and Porrini (1997) and chromatographic conditions were established by Yeum et al. (1996). Lycopene is a nonpolar soluble substance with a retention time 33 min in HPLC (Fig. 5.3).

5.4 Lycopene and Diseases

Given the importance of oxidative stress in the pathogenesis of chronic diseases, several therapeutic strategies using antioxidants have been tested with the aim of reducing reactive oxygen species (ROS) and nitrogen (RNS) overproduction (Ford et al. 2005). Various observational studies have shown that diets rich in fruits and vegetables are correlated with reduced risk of chronic diseases onset (Hung et al. 2008; Neuhouser et al. 2002). Thus, it is likely that antioxidant nutrients present in these foods can prevent damage caused by ROS and RNS.

There is a positive correlation between lycopene intake and health. It plays an important role in preventing several diseases, including cancers. Lycopene is the most efficient oxygen and free radicals scavenger among carotenoids. Moreover, it controls cell cycle and activates phase II detoxification enzymes. Epidemiological studies confirm its significant role in the diseases preventing (Bramley 2000). An important and prospective cohort study of 47,367 U.S. male health professionals (dentists, optometrists, osteopaths, podiatrists, pharmacists, and veterinarians), aged 40–75, were followed for 12 years. During this period, 2,481 men developed prostate cancer. Results showed that frequent tomato sauce intake was associated

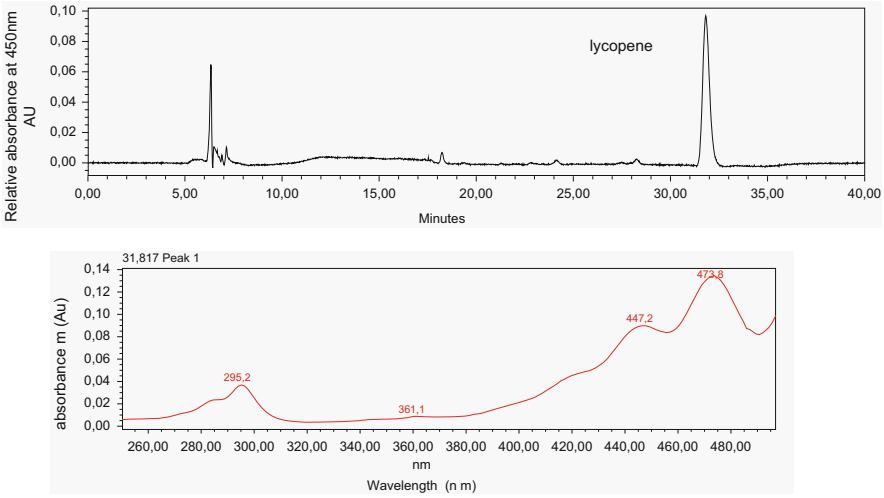

Fig. 5.3 Lycopene extracted from tomatoes by HPLC at 450 nm with its respective spectrum

with a great reduced risk of prostate cancer (organ-confined, advanced, or metastatic). Interestingly, the authors did not observe a substantial association between tomato sauce intake and risk of prostate cancer in men diagnosed when younger than 65 years. Possibly, prostate cancers presenting at an early age may represent an accelerated process of carcinogenesis influenced more by genetic or endogenous factors (Giovannucci 1999).

The relation between lycopene and cardiovascular disease has been examined in several epidemiological studies (Wu et al. 2003; Kardinaal et al. 1993; Kohlmeier et al. 1997; Kristenson et al. 1997). Lycopene protection against the oxidation of DNA bases has recently been demonstrated in cardiomyocytes from rats subjected to cardiotoxicity and supplemented with lycopene in oleoresin (Ferreira et al. 2007b). Examining men ($\leq$70 years) from ten European countries, an important study showed an inverse association between risk of acute myocardial infarction (AMI) and adipose tissue level of lycopene. The results also showed that lycopene was the only carotenoid with independent association for low risk of AMI (Kohlmeier et al. 1997). Other authors reported decreased lycopene levels in plasma from patients (men and women, average age 55 years) with dyslipidemia (total cholesterol $\geq$ 240 mg/dL; triglycerides $\geq$ 250 mg/dL) (Araujo et al. 1995). The effect of supplementation with lycopene in attenuating disease has also been examined. In men (30–35) supplemented with lycopene (60 mg/day/3 months), a study showed a significant reduction in plasma LDL. The authors also showed that the addition of lycopene to a macrophage culture resulted in decreased synthesis of important coenzyme in cholesterol [3 macrophage-hydroxy-3-methyl glutaryl coenzyme A (HMGCoA) reductase] (Fuhrman et al. 1997). Supplementation with lycopene as tomato extract (15 mg licopeno/day/8 weeks) resulted in improvement of systolic and diastolic pressure and LDL oxidation (induced by $CuSO_4^{-}$) of

patients (30–70 years) with hypertension (Engelhard et al. 2006). Another study has showed that there was no effect on DNA damage after supplementation of individual carotenoids (15 mg/12 weeks of α/β carotene, lutein, or lycopene) in men and women (25–45 years) as compared with placebo group. However, there was interesting inverse correlation between serum carotenoids and oxidized pyrimidines (Collins et al. 1998). Another study using the same amount of carotenoids adopted by Collins and collaborators (Collins et al. 1998) during shorter period (1 week) showed a significant increase in DNA repair in young women (24–34 years) after individualized supplementation with lutein, carotene, or lycopene (Zhao et al. 2003). Men and women with normal BMI who made use of Lyco-O-Mato 6 % oleoresin (5–7 mg of lycopene) for 26 days showed significant reduction in DNA damage in lymphocytes subjected to oxidative stress (Porrini et al. 2005).

An experimental study found that lycopene (at doses of 10, 30, 60, and 90 mg/kg) administered to adult hyperglycemic Sprague Dawley rats resulted in several improvements (decreased glucose and lipid peroxidation; increased insulin and antioxidant enzymes) in a dose-dependent manner (Ali and Agha 2009). The results suggest that supplementation with lycopene can contribute to attenuation of oxidative stress in this model. Adult hyperlipidemic Sprague Dawley rats supplemented with tomato powder, paste, and ketchup (10 or 20 mg lycopene/kg diet) showed improvement in all lipid parameters. In addition, this study demonstrated that the lowest dose of lycopene (10 mg/kg diet) tomato paste achieved a better atherogenic index and a significant increase in high density lipoprotein cholesterol (HDL) in these animals (Ibrahim et al. 2008). In a model of ischemia and reperfusion in the heart from adult Wistar rats was observed that lycopene decreased the damage caused by lipid peroxidation, increased the concentration of antioxidant enzymes, and improved hemodynamic parameters by suppressing oxidative stress and reducing myocardial injury (Bansal et al. 2006). In hypercholesterolemic mice was observed that the concentrate tomato juice added to the diet (20 g of lycopene/100 g diet) prevented atherosclerosis by protecting the plasma lipid oxidation (Suganuma and Inakuma 1999).

Besides acting as an antioxidant, lycopene has also been reported to display anti-inflammatory effects in adipocytes (Marcotorchino et al. 2012) and liver (Bignotto et al. 2009). Evidence is increasing that lycopene or tomato preparations can lower inflammatory markers (Hung et al. 2008; Gouranton et al. 2011; Ghavipour et al. 2012) and may improve diseases with chronic inflammatory backgrounds such as obesity (Ghavipour et al. 2012). Such anti-inflammatory role of lycopene in adipocytes was demonstrated by its inhibitory action on the transcription factor kappa B in producing pro-inflammatory cytokines (Bramley 2000).Our recent study have also showed lycopene supplementation (10 mg lycopene/kg body wt/day/6 weeks) significantly decreased leptin, resistin, and IL-6 gene expression in adipose tissue and in plasma concentrations from obese animals (Luvizotto et al. 2013), suggesting that dietary lycopene may be proposed as an effective strategy to reduce the inflammation in obesity.

Lycopene is a carotenoid that has recently received considerable attention, and it is hypothesized to play a preventative role in a variety of diseases. Although the

chemistry and in vitro properties of lycopene have been known for several years, little is known about its biodistribution, metabolism, and bioavailability in humans and its bioactivity. The products derived from tomatoes are the richest source of lycopene and ripening and cooking in oil medium are factors that enhance its bioavailability. However, current knowledge of the bioavailability of lycopene in humans is limited due to the inability to distinguish newly administered lycopene from the body reserves of lycopene. Thus, research utilizing labeled tomato will contribute to clarify the lycopene effect on nutritional modification and disease prevention. Although several questions still remain to be answered, it would be prudent to consider including dietary lycopene as part of a healthy diet.

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