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Review Article

LYCOPENE- SECONDARY SUPPRESER FOR CANCER

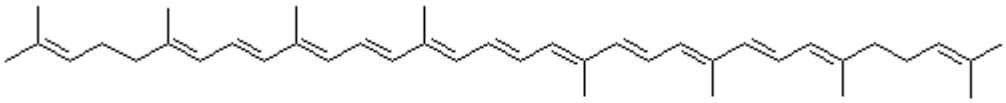
GP. Bhagath Singh and Pasumarthi Prasanth

Donbosco P.G. College of Pharmacy, 5th mile, Pulladigunta, Vatticherukuru, Guntur, Andhra Pradesh, India.

ABSTRACT

Lycopene, the most predominant carotenoid belongs to the same family as β-carotene, is what gives tomato and many other fruits their red colour. It is a phytochemical, synthesized by only plants and micro-organisms. It is a powerful antioxidant which can neutralize the free radicals with the unique eleven conjugated bonds in its chemical structure thereby conferring protection against prostate cancer, breast cancer, atherosclerosis, and associated coronary artery diseases along with oral leukoplakia. It reduces LDL (low density lipoprotein) oxidation thus reducing cholesterol levels in the blood. In addition, research suggests that lycopene reduces the risk of macular degenerative disease, serum lipid oxidation and cancers of the lung, bladder, cervix and skin. The chemical properties and the various mechanisms of actions of lycopene are well documented in this review.

INTRODUCTION



Lycopene

Molecular Weight = 536.89
Exact Mass = 536
Molecular Formula = C40H56
Molecular Composition = C 89.49% H 10.51%

Lycopene, a carotenoid found in tomato products, prevents oxidation of low density lipoprotein (LDL) cholesterol and reduces the risk of developing atherosclerosis and coronary heart disease according to a recent study published in the October 1998 issue of Lipids. **The studies by Agarwal et al. showed that daily consumption of tomato products providing at least 40 mg of lycopene was enough to substantially reduce low density lipoprotein (LDL) oxidation.** High LDL oxidation is associated with increased risk of atherosclerosis and coronary heart disease. This lycopene level can be achieved by drinking just two glasses of tomato juice a day. Research shows that lycopene in tomatoes can be absorbed more efficiently by the body if processed into tomato juice, sauce, paste and ketchup. The bound chemical form of lycopene found in tomatoes is converted by the temperature changes involved in processing to make it more easily absorbed by the body.[1]

Although best known as an antioxidant, both oxidative and non-oxidative mechanisms are

involved in lycopene's bioprotective activity. The nutraceutical activities of carotenoids such as beta-carotene are related to their ability to form vitamin A within the body. Since lycopene lacks a beta-ionone ring structure, it cannot form vitamin A and its biological effects in humans have been attributed to mechanisms other than vitamin A. Lycopene's configuration enables it to inactivate free radicals. As free radicals are electrochemically imbalanced molecules, they are highly aggressive, and are always 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 ten times higher than that of alpha-tocopherol (vitamin E relative). One non-oxidative activity is, the regulation of gap-junction communication between cells. **Lycopene is a phytochemical, synthesized by plants and microorganisms but not by animals. It is an acyclic isomer of beta-carotene.**

Research shows that lycopene in tomatoes can be absorbed more efficiently by the body if processed into tomato juice, sauce, paste and ketchup. The bound chemical form of lycopene found in tomatoes is converted by the temperature changes involved in processing to make it more easily absorbed by the body. The research results prove that lycopene can reduce the risk of prostate cancer and cancers of the lung, bladder, cervix and skin. [2]

Supplementation of tomato products, containing lycopene, has been shown to lower biomarkers of oxidative stress and carcinogenesis in healthy and type II diabetic patients, and prostate cancer patients, respectively. Processed tomato products like tomato juice, tomato paste, tomato puree, tomato ketchup and tomato oleoresin have been shown to provide bioavailable sources of lycopene, with consequent increases in plasma lycopene levels versus baseline. Dietary fats enhance this process and should be consumed together with food sources of lycopene.

An increased oxidative stress has been implicated in the incidence of chronic diseases. Dietary intakes of tomatoes and tomato products containing lycopene have been associated with a decreased risk of diseases such as cancer and cardiovascular diseases (CVDs) in numerous studies. [3] Tomatoes account for 85% of lycopene consumption in an average American diet, and is an essential component of the Mediterranean diet, which is well known for its cardioprotective and anticarcinogenic health effects.[4]

Tomatoes are a valuable source of several micronutrients and phytochemicals including carotenoids, polyphenols, potassium, folate, ascorbic acid and a-tocopherol. Most of these nutrients in tomatoes can interact with the host to confer a preventive benefit against oxidative stress-associated diseases, through various mechanisms including antioxidant action[5]

As metioned earlier that lycopene can be absorbed more efficiently by the body after it has been processed into juice, sauce, paste, or ketchup. In coming to fresh fruit, lycopene is enclosed in the fruit tissue. Therefore, only a portion of the lycopene that is present in fresh fruit is absorbed. Processing fruit makes the lycopene more bioavailable by increasing the surface area available for digestion. More significantly, the bound chemical form of lycopene is altered by the temperature changes involved in processing to make it more easily absorbed by the body. Also, because lycopene is fat-soluble (as are vitamins, A, D, E, and beta-carotene), absorption into tissues is improved when oil is added to the diet. Research has shown convincing evidence regarding the isomerization of all trans-isomers to cis-isomers, under acidic conditions of the gastric juices.[6]

One of the most influential pieces of research on tomatoes and cancer was a done by Harvar, released in 1995. It followed the eating habits of 47,000 men for six years. Those who had at least 10 weekly servings of tomato-based foods were up to 45 percent less likely to develop prostate cancer. In an analysis published by J Natl Cancer Inst 1999 Feb 17;91(4):317-31), Edward Giovannucci of Harvard Medical School reviewed 72 studies that looked for a link between cancer risk and food made with tomatoes. In all, 57 linked tomato intake with a reduced risk, and in 35 of these, the association was strong enough to be considered statistically meaningful.

The consumption of tomato products may reduce the susceptibility of lymphocyte DNA to oxidative damage. Tomato has a preventive effect on atherosclerosis by protecting plasma lipids from oxidation.

BIOAVAILABILTY OF LYCOPENE

When a dietary supplementation of tomato puree for 2 weeks in healthy volunteers was given, it led to a completely different isomer pattern of plasma lycopene in these volunteers, versus those present in tomato puree. 5-cis, 13-cis and 9-cis-lycopene isomers, not detected in tomato puree, were predominant in the serum.[6]

Studies conducted with lymph cannulated ferrets have shown better absorption of cis-isomers and their subsequent enrichment in tissues.

One of the convincing evidence regarding the isomerization of all trans- lycopene to cis-isomers, under acidic conditions of the gastric juice is, when Incubated lycopene derived from capsules with simulated gastric juice for 1 min showed a 40% cis-lycopene content, whereas the levels did not exceed 20% even after 3 hour incubation with water as a control. However, when tomato puree was incubated for 3 hour with simulated gastric juice, the cis-lycopene content was only 18%, versus 10% on incubation with water. Thus, gastric Ph and food matrix influence isomerization and subsequent absorption and increased bioavailability of cis-lycopene. [7]The process of cooking which releases lycopene from the matrix into the lipid phase of the meal, increases its bioavailability, and tomato paste and tomato puree are more bioavailable sources of lycopene than raw tomatoes.[8]

Factors such as certain fibers, fat substitutes, plant sterols and cholesterol-lowering drugs can interfere with the incorporation of lycopene into micelles, thus lowering its absorption [9]. Several clinical trials have also shown the bioavailability of lycopene from processed tomato products. There were reports of a significant increase in serum lycopene levels following a 1-week daily consumption of spaghetti sauce (39mg of lycopene), tomato juice (50mg of lycopene) or tomato oleoresin (75 or 150mg of lycopene), in comparison with the placebo, in healthy human volunteers. There was also other indication that the lycopene levels increased in a dose-dependent manner in the case of tomato sauce and tomato oleoresin[1].

There were further demonstrations that enrichment of tomato paste with 6% tomato peel increases lycopene bioavailability in men, thereby suggesting the beneficial effects of peel enrichment, which are usually eliminated during tomato processing[10].

One of the researchers compared the bioavailability of lycopene from tomato paste and from lactolycopene formulation (lycopene from tomato oleoresin embedded in a whey protein matrix), and reported similar bioavailability of lycopene from the two sources in healthy subjects. Dietary fat has been shown to promote lycopene absorption, principally stimulating bile production for the formation of bile acid micelles[11].

Consumption of tomato products with olive oil or sunflower oil has been shown to produce an identical bioavailability of lycopene, although plasma antioxidant activity improved with olive oil consumption, suggesting a favorable impact of monounsaturated fatty acids on lycopene absorption and its antioxidant mechanism.

In many of one interesting studies conducted there were reports that Avocado lipids play a role in enhancing lycopene absorption. In this study, in healthy, nonpregnant, nonsmoking adults, the addition of avocado fruit (75 or 150 g) or avocado oil (12 or 24 g) to salsa (300 g) enhanced lycopene absorption, resulting in 4.4 times the mean area under the concentration-versus-time curve after intake of avocado-free sauce. That study demonstrated the favorable impact of avocado consumption on lycopene absorption and has been attributed to the fatty acid distribution of avocados (B66% oleic acid), which may facilitate the formation of chylomicrons[1].

Summary of clinical trials investigating the effects of supplementation of tomato products, tomato oleoresin or purified lycopene on biomarkers of oxidative stress and carcinogenesis.

Study	Subjects	Type and duration of lycopene supplementation	Effects on biomarkers of oxidative stress/carcinogenesis	Effects on plasma lycopene levels
Agarwal and Rao (1998)	19 healthy subjects (mean age 29 years, BMI 24+_1.5 kg/m^2)	0 mg lycopene (placebo), 39 mg lycopene (spaghetti sauce,), 50 mg lycopene (tomato juice), or 75 mg lycopene (tomato oleorisin) per day for 1 week	25% decrease in LDL-TBARS 13% decrease in LDL-CD for all groups versus placebo ($p<0.05$)	Increases at 7 days in all groups versus placebo ($p<0.05$)
Riso *et al.*(1999)	10 healthy subjects (mean age 23.1+_1.1 years, BMI 20.5+_1.5 kg/m^2)	16.5 mg lycopene (60 g tomato puree), per day for 21 days	38% decrease in Dna damage in lymphocytes ($p<0.05$)	Increase at 21 days versus baseline ($p<0.001$)
Bub *et al.* (2000)	23 healthy volunteers (mean age 34+_4 years, BMI 23+_2 kg/m^2)	40 mg lycopene (330 ml tomato juice) for 2 weeks	12% decrease in plasma TBARS 18% increase in LDL lag time ($P<0.05$) no effects on water-soluble antioxidants, FRAP, glutathione peroxidases and reductase activities ($p>0.05$)	Increase at 2 weeks versus baseline ($p<0.05$)
Chopra *et al.*(2000)	34 healthy females (mean age 37.5+_8.5 years, BMI 24+_3.5 kg/m^2)	>40 mg lycopene (200 g tomato puree + 100 g watermelon) per day for 7days	Significant decrease in LDL oxidizability in nonsmokers ($p<0.05$); no effects in smokers ($p>0.05$)	Increase at 7 days versus baseline ($p<0.05$)
Poorini and Riso (2000)	9 healthy subjects (mean age 25.4+_2.2years, BMI 20.3+_1.5 kg/m^2)	7 mg lycopene (25 g tomato puree), per day for 14 days	50% decrease in DNA damage in lymphocytes ($p<0.05$)	Increase at 14 days versus baseline ($p<0.001$)
Upritchard *et al.*(2000)	15 well-controlled type II diabetics (mean age 63_+8years, BMI 30.9+_7 kg/m^2)	Tomato juice (500ml) per day or placebo for 4 weeks)	Decreased LDL oxidizability versus baseline ($p<0.001$)	Increase at 4 weeks versus baseline ($p<0.001$)
Hininger *et al.* (2001)	175 healthy volunteers (mean age 33.5+_1 years, BMI-24.3+_0.5 kg/m^2)	15 mg lycopene (natural tomato extract) or placebo per day for 12 weeks	No effects on LDL oxidation, reduced hlutathione, protein SH groups and antioxidant metalloenzyme activcities ($p>0.05$)	Increase at 12 weeks versus baseline ($p<0.05$)
Chen *et al.* (2001)	32 patients with localiszed prostate adenocarcinoma (mean age 63.7_+6.1 years,BMI 28.0+_4.9 kg/m^2)	30 mg lycopene (200 g spaghetti sauce) per day for 3 weeks before surgery or a reference group with no supplementation	Decreased leukocyte and prostate tissue oxidative DNA damage; decreased serum PSA levels ($p<0.05$)	Increase at 3 weeks versus baseline ($p<0.001$)
Kucuk *et al.* (2001)	26 patients with newly diagonsed, clinically localized prostrate cancer (mean age 62.15_+1.85 years, BMI not reported)	15 mg lycopene (Lyc-O-Mato capsules) twice daily or no supplementation for 3 weeks before surgery	Decreased tumor growth in the intervention group versus control ($p<0.05$); decreased plasma PSA levels and increased expression of connexin 43 in prostrate tissue in the intervention group versus control ($p>0.05$); decreased plasma IGF-1 levels in intervention and control groups ($p<0.05$)	No effects at 3 weeks versus baseline ($p>0.05$)
Porrini *et al.* (2002)	9 healthy subjects (mean age 25.2+_2.2 years, BMI 20.2+_1.6 kg/m^2)	7 mg lycopene (25 g tomato puree) with 150 g of spinach and 10 g of olive oil per day for 3 weeks	Decreased DNA oxidative damage ($p<0.05$)	Not reported
Rao and Shen (2002)	12 healthy subjects (mean age 31+_2.7 years, BMI 22.6+_1.2 kg/m^2)	5,10,20 mg of lycopene from tomato ketchup or Luc-O-Mato capsule per day for 2 weeks	10% decrease in serum MDA 23.6% increase in reduced thiols ($p<0.05$)	Increase at 2 weeks versus baseline ($p<0.05$)
Kiokias and Gordan	32 healthy volunteers (mean age 31.7+_11.3	4.5 mg lycopene (as Lyc=O-Mato, in combination with beta-	Decreased LDL oxidizability; ($p<0.05$) but nonsignicificant decrease in DNA damage (8-hydroxy-2-deoxyguanosine in urine) in	Increase at 3 weeks versus baseline ($p<0.05$)

(2003)	years, BMI 22.4+_3.0 kg/m^2)	carotene, alpha-carotene, bixin, lutein, and paprika carotenoids) = 4 g fish oil, only; per day for 3 weeks	carotenoid group + fish oil versus fish oil only	
Hadley *et al.* (2003)	60 healthy subjects (mean age 52.6+_1.8 years, BMI not reported)	35 mg lycopene (condensed tomato soup), 23mg lycopene (ready to serve tomato soup), or 25 mg lycopene (v8 vegetable juice), per day for 15 days	Increase in LDL lag time in all groups ($p<0.05$) No effects on urinary 8-hydroxy-2-deoxyguanosine or urinary F_2-isoprostanes	Increase at 15 days versus baseline ($p<0.05$)
Visioli *et al.*(2003)	12 healthy subjects (mean age 30 years, BMI 21 kg/m^2)	8 mg lycopen (tomato products: raw tomatoes, tomato sauce, tomato paste), with 5 g olive oil per day for 3 weeks (21 days)	Decrease in LDL oxidizibility; Decrease in excretion of urinary F_2-isoprostanes ($p<0.05$)	Increase at 3 weeks versus baseline ($p<0.05$)
Briviba *et al.* (2004)	22 healthy men (mean age and BMI not reported)	37 mg lycopene (330 ml of tomato juice) for 2 weeks	No effects no lipid peoxidation in plasma and feces ($p>0.05$)	Increase at 2 weeks versus baseline ($p<0.001$)
Riso *et al.*(2004)	12 healthy subjects (mean age 25.2+_4.3 years,BMI 20.6+_1.8 kg/m^2)	8 mg lycopene (100 g raw tomatoes, 60 g tomato sauce, 15 g tomato paste) per day for 3 weeks	Decreased DNA oxidative damage ($p<0.05$); No effects on lymphocyte MDA levels ($p>0.05$)	Increase at 3 weeks versus baseline ($p<0.001$)
Rao (2004)	17 healthy subjects	30 mg lycopene (tomato juice, tomato sauce, tomato paste, ketchup, spaghetti sauce, and ready-to-serve tomato soup) per day for 4 weeks	Decrease lipid and protein oxidation ($p<0.05$)	Increae at 4 weeks versus baseline ($p<0.05$)
Porrini *et al. (2005)*	26 healthy subjects (mean age 25.8+_2.8 years, BMI 21.3+_1.7 kg/m^2)	5.7 mg lycopene (Lyc-O-Mato, 250 ml), or placebo drink, per day for 26 days	42% decrease in DNA damage in lymphocytes ($p<0.05$)	Increase at 26 days versus baseline ($p<0.0001$)
Bub *et al.* (2005)	22 healthy volunteers with different PON1-192 genotypes (mean age 29+_6 years,BMI23+_2 kg/m^2)	37 mg lycopene (330 ml of tomato juice) per day for 2 weeks		
Zhao *et al. (2006)*	37 healthy nonsmoking plstmenopausal women (mean age 60+_2 years, BMI 25.48+_1.08 kg/m^2)	12 mg of synthetic lycopene, or 4 mg of synthetic lycopene as part of mixed caroteniods, or placebo, per day for 56 days	Decreased endogenous DNA damage in both carotenoid supplemented groups versus baseline and placebo ($p<0.01$)	Increase at 56 days versus baseline in lycopene only supplemented group ($p<0.01$)

Abbreviations: BMI-body mass index; LDL-low density lipoprotein; TBARS-thiobarbituric acid reactive substances; CD-conjugated diene; MDA-malondialdehyde.

Mechanism of action of Lycopene

Cellular and molecular studies have shown lycopene to be one of the most potent antioxidants and have been suggested to prevent carcinogenesis and atherogenesis by protecting critical biomolecules such as DNA, proteins, lipids and low-density lipoproteins (LDLs)[13].

Lycopene, because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability compared to b-carotene or a-tocopherol. Cis- lycopene has been shown to predominate in both benign and malignant prostate tissues, suggesting a possible beneficial effect of high cis-isomer concentrations, and also the involvement of tissue isomerases in in-vivo isomerization from all Trans to cis form [14].

At a physiological concentration of 0.3 mol/l, lycopene has been shown to inhibit growth of

non-neoplastic human prostate epithelial cells in vitro, through cell cycle arrest which may be of significant implications in preventing benign prostate hyperplasia, a risk factor for prostate cancer[15].

Lycopene has also been shown to significantly reduce LNCaP human prostate cancer cell survival in a dose-dependent manner, and this antineoplastic action may be explained by increased DNA damage at high lycopene concentrations (45 mM), whereas lower levels of lycopene reduced malondialdehyde formation, with no effects on DNA[16].

However, in the Dunning rat prostate cancer model, a 4-week supplementation with a higher concentration of lycopene beadlets (4 g lycopene/kg diet), revealed significant down regulation of 5-a-reductase, reduced steroid target genes expression and prostatic insulin-like growth factor-1 (IGF-1) and Interleukin- 6, thereby causing a subsequent reduction in the growth of tumor tissue [17]. As evident from in vitro and animal studies, purified lycopene may inhibit prostate cancer growth only at higher concentrations, in comparison with tomato antioxidant supplementation [18].

The further studies have reported the inhibitory effects of lycopene on MCF7 human mammary cancer cell growth, owing to interference in IGF-1 receptor signaling and cell cycle progression. Thus, interference in androgen metabolism, and inhibition of growth factors and cytokine activity, appear to be the major pathways through which lycopene inhibits prostate and breast cancer growth. Tomato lycopene supplementation (1.1 mg/kg/day corresponding to 15mg lycopene intake in a 70 kg person) has also been shown to prevent the change in p53, p53 phosphorylation and p53 target genes, induced by cigarette smoke exposure in the gastric mucosa of ferrets. This further suggests a protective effect of lycopene against the development of gastric cancer[19]. Studies using human and animal cells have identified a gene, connexin 43, correlated with reduced indexes of neoplasia, and whose expression is upregulated by lycopene and which allows direct intercellular gap junctional communication, thereby reducing the rate of proliferation[20].

Lycopene has also been shown to interfere in lipid metabolism, lipid oxidation and corresponding development of atherosclerosis. Lycopene treatment has been shown to cause a 73% suppression of cellular cholesterol synthesis in J-774A.1 macrophage cell line, and augment the activity of macrophage LDL receptors [21].

Tomato product supplementation and biomarkers of oxidative stress and carcinogenesis: clinical trials in healthy subjects, type II diabetic patients and prostate cancer patients

The above table summarizes the clinical trials investigating the effects of supplementation of tomato products or tomato oleoresin, containing lycopene, on biomarkers of oxidative stress and carcinogenesis. Several studies have shown that the antioxidant effects of supplementation of tomato products or purified lycopene (providing 6–17mg lycopene/day), on cellular DNA, in healthy human volunteers[22].

A study in the year 2005 involving a 2-week supplementation of tomato juice of 37mg of lycopene/day, showed a reduced lipid peroxidation in healthy men carrying the R-allele of the PON1-192 genotype, compared to QQ subjects. These volunteers with the QR/RR genotype also showed an increased lipid peroxidation at baseline as compared to subjects. These studies reveal that the dose and duration of tomato lycopene supplementation, the synergistic action of lycopene with natural carotenoids, the baseline plasma levels of lycopene, the choice of biomarkers of oxidative stress and gene polymorphisms affecting the rate of oxidative stress are critical factors in modulating the response to antioxidant supplementation, containing lycopene, in healthy volunteers[23].

Epidemiologic studies: lycopene, CVD and cancer

The European Multicenter Case–Control Study on Antioxidants, Myocardial Infarction and Breast Cancer Study (EURAMIC Study) reported that a higher lycopene concentration was independently protective against CVD [24].

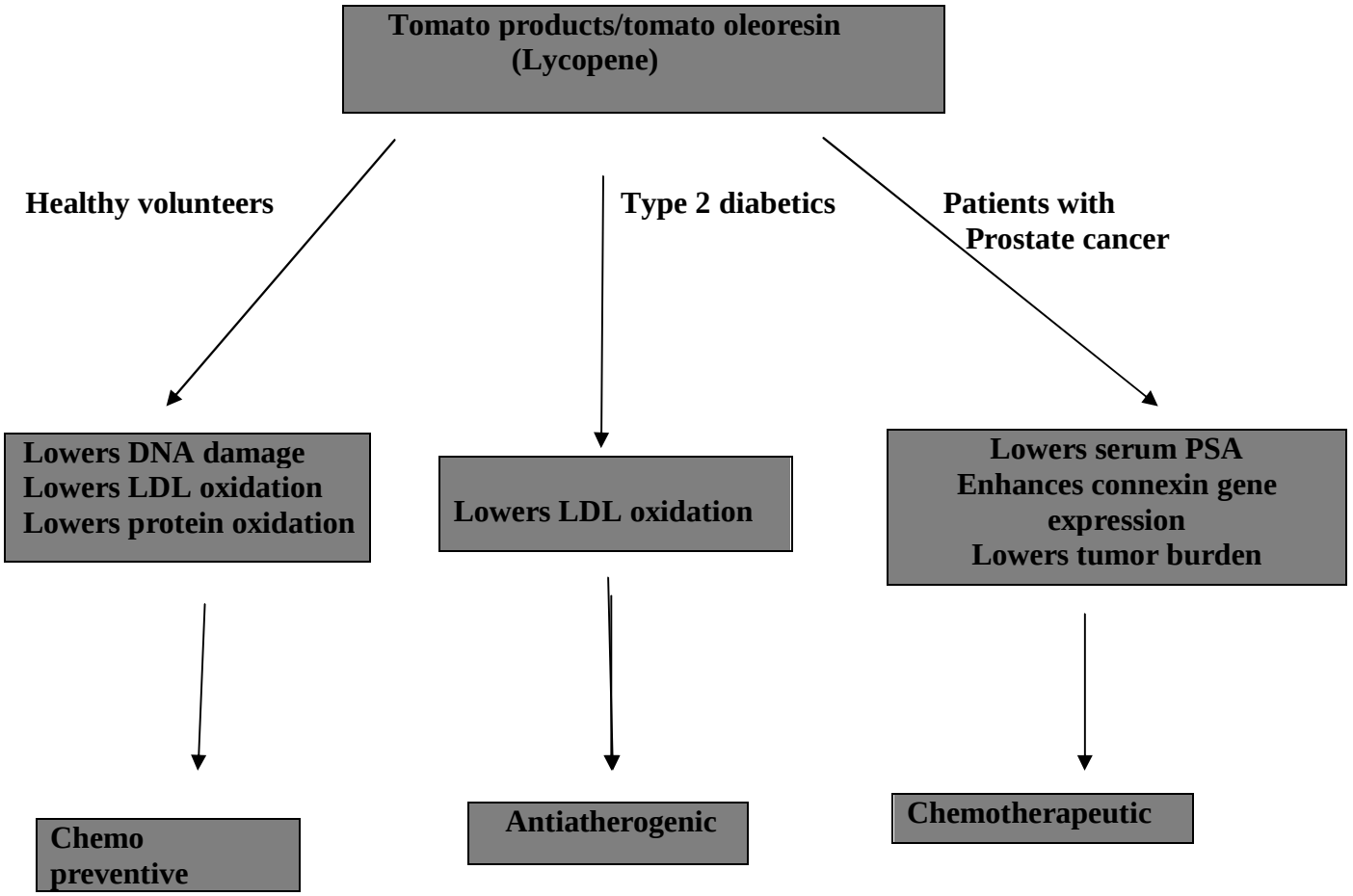
The Women's Health Study further revealed that a decreased risk for developing CVD was more strongly associated with higher tomato intake than with lycopene intake[25].

Processed tomato products definitely provide a bioavailable source of lycopene and have a positive correlation with plasma and tissue lycopene levels.

A systematic review of 72 epidemiological studies reported a consistent inverse relationship between intakes of tomatoes and plasma lycopene levels and prostate, lung and stomach

cancer[26]. In the meta-analysis, 10 out of 14 studies reported a significant inverse association between tomato or lycopene consumption and lung cancer risk. These were case–control studies, adjusted for smoking history, an important confounding factor for lung cancer.

In the Health Professionals Follow-Up Study, an intake of X2 servings a week of tomato products resulted in a lower risk of prostate cancer[27]. Using plasma samples from men enrolled in the Physicians' Health Study, lycopene was found to be the only antioxidant at significantly lower levels in prostate cancer cases than in the matched controls. This inverse association was particularly evident for aggressive types of prostate cancer and for men not taking b-carotene supplements[28].



Summary of mechanism of action of tomato products or tomato oleoresin supplements, containing lycopene,in health and disease.

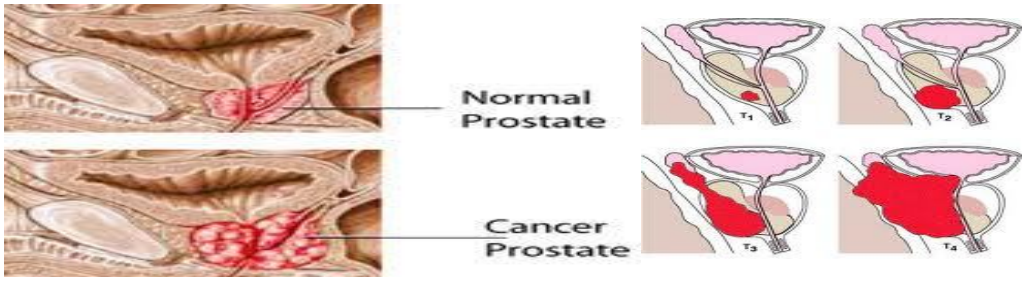
In prevention of prostate cancer

Lycopene inhibits the growth of benign and malignant prostatic epithelial cells in vitro.

Lycopene has many effects like anti-proliferative insulin like growth factor-1 inhibition, differentiation and apoptosis, connexin and gap junctional intercellular communication and its antioxidant activation plays role in carcinogenesis inhibition[29]. Mohanty one of the researcher undertook a study to use lycopene as a chemo preventive agent in the treatment of HGPIN for preventing prostate cancer from

developing in this vulnerable group of patients. A total of 40 patients with HGPIN were randomized into 2 groups: one received 4mg lycopene twice a day for one year, and the other was periodically followed up one year. PSA level in the treated group A decreased for a mean level of 6.07–3.5 ng/ml, while in the control group B, it increased from a mean value of 6.55 to 8.06 ng/ml. This initial small trial has shown that lycopene is an effective chemo preventive agent in preventing HGPIN from becoming prostate cancer[30].

Health Professionals Follow-Up Study demonstrating that lycopene intake was associated with a significant decrease risk of prostate cancer (RR=0.84, 95% Cl 0.73- 0.96, p=0.003) and greater reduction in risk for extra prostatic disease[31].



Normal prostate and Cancer Prostate representation pictorially

A prospective study demonstrated that frequent consumption (>1/day) of soy milk was associated with a 70% reduction in the risk of developing prostate cancer[32].

Sources of Dietary Agents and Chemo preventive Mechanisms

Agent	Sources	Chemoprevention mechanisms
Lycopene	Tomato, watermelon, guava, pink grape.	Antioxidant activation,IGF-1 inhibition, promoting apoptosis
Isoflavonoids	Soybean, legumes, green tea	Inhibit cell growth, down-regulation androgen, and estrogen-like activity.
Selenium	Fish , meat, eggs	Induce antioxidant enzymes, promote apoptosis, and inhibit cell growth.

In treating Oral Leukoplakia

Leukoplakia is the most common pre-cancerous lesion in the oral cavity. Malignant potential of leukoplakia was hinted by Sugar and Banoczy way back in 1957[33]. Association between tobacco chewing and smoking with oral leukoplakia is established beyond doubt[34-35].Tobacco smoke contains NOO_ radicals, which are carcinogenic. Free radical scavengers should be the necessary part of the treatment regimen in tobacco chewers or smokers to prevent the formation, induce the remission or inhibit the progression of pre-cancerous lesions into malignancies. Lycopene, the carotenoid that gives the ripe tomato its bright red color, is a very effective natural antioxidant and quencher of free radicals [36].

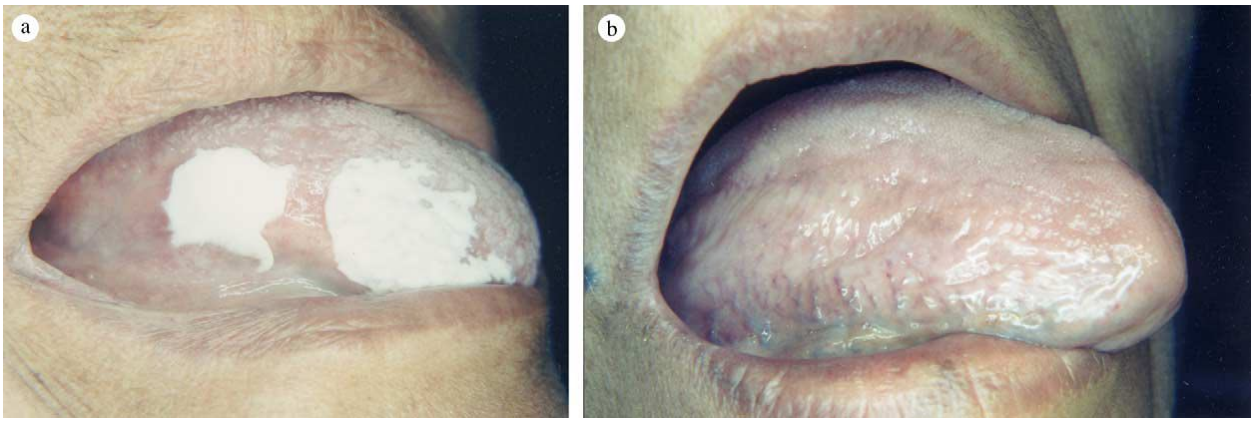
Lycopene exhibits the highest physical quenching rate constant with singlet oxygen [14].

Lycopene has been found to be at least 3-fold more effective than b-carotene in preventing cell death by quenching of NOO_radicals [37]. It also protects DNA damage induced by 1-methyl-3 nitro-1-nitrosoguanidine and H_2O_2 [38].

Lycopene also increases the expression of a gene encoding connexin-43, a gap junction protein, effect being independent of pro vitamin-A or antioxidant properties[39].

Lycopene and b-carotene are two major carotenoids found in human buccal mucosal cells. Protective effect of tomato consumption has been observed in oral leukoplakia in a population based case control study [40]. Tomato, tomato products and lycopene consumption is associated with reduction in upper aero-digestive tract cancers like oral cavities, pharynx, larynx and oesophagus[41]. Administration of lycopene suppresses DMBA-induced oral carcinogenesis[42].

The first report of efficacy of lycopene against human oral cancer cell was recently published describing the significant therapeutic effect [43].



(a) Before starting 8 mg lycopene therapy. **(b) Complete response seen after 8 mg lycopene therapy.**

Other irrefutable effects of Lycopene

- Studies prove that it has been useful in lowering of hypertension, in particular mild hypertension.
- Naturally lycopene is useful in the production of vitamin A. So, it is also helpful in improving eyesight.
- Lycopen increases the High Density Lipid Levels (HDL) which is useful for the absorption of Lower Density Lipids (LDL), thereby preventing Atherosclerosis and Hypercholestremia. As an anti-oxidant it also helps cholesterol from being oxidized.
- Lycopene is also useful in treating oral Leukoplakia, a condition which is precancerous mucous membrane, which is manifested by white patches mainly due to the frequent consumtion or chewing of tobacco.

Supplements of Lycopene

		Amount		Amount
Food	**Food form**	**(mg/100g)**	**mg per serving**	**Serving size**
Apricots	Fresh	0.005	0.007	140 g
Apricots	Canned, drained	0.065	0.091	140 g
Chilly	Processed	1.08-2.62	1.40-3.41	130 g
Grapefruit	Pink, fresh	3.36	4.7	140 g
Guava	Pink, fresh	5.4	7.56	140 g
Guava juice	Pink, processed	3.34	8.35	240 ml-250 g
Ketchup	Processed	16.6	3.32	1 tbsp.-20 g
Papaya	Red, fresh	2.00-5.30	2.8-7.42	1409
Pizza sauce	Canned, drained	12.71	15.89	125 g
Rosehip puree	Canned, drained	0.78	0.47	60 g
Spaghetti sauce	Processed	17050	21.88	125 g
salsa	Processed	9.25	3.71	2 tbsp. - 40 g
Tomatoes	Red, fresh	3.1 - 7.74	4.03 - 10.06	130 g
Tomatoes	Peeled, processed	11.21	14.01	125 g

Tomato juice	Processed	7.83	19.58	240 ml-250 g
Tomato soup	Canned, condensed	3.99	9.77	245 g
Tomato paste	Canned	30.07	9.02	30 g
Watermelon	Red, fresh	4.1	11.48	280 g
Vegetable juice	Processed	7.28	17.47	240 ml-250 g

Handiness and Dosage

Lycopene is formulated along with the multivitamins. They are formulated as capsules. An intake of 5-10 mg, few times a week is ample for the ones who do not take much more vegetables or fruits. But for those who have a decent diet of fruits and vegetables there isn't any need of running for dietary supplemnts of lycopene. And there are many lycopene products available in the day to day market in the form of syrups and capsules.

CONCLUSION

Thus, it can be concluded that moderate amounts of whole food-based supplementation of tomato soup, tomato puree, tomato juice or other tomato beverages, consumed with dietary fats, such as olive oil or avocados, leads to increase in plasma carotenoids, particularly lycopene. And there are much epidemiological evidence that lycopene consumption is associated with a lower risk of prostate, gastric, breast cancers and many more which has been shown up in this article.

So considering all the above information produced, an everyday intake of lycopene is adviced.

This article evokes that it is better to have lycopene supplements than to fall in the risk for surgeries and other various treatments.

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