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To cite this article: Rashida Perveen, Hafiz Ansar Rasul Suleria, Faqir Muhammad Anjum, Masood Sadiq Butt, Imran Pasha & Sarfraz Ahmad (2015) Tomato (*Solanum lycopersicum*) Carotenoids and Lycopenes Chemistry; Metabolism, Absorption, Nutrition, and Allied Health Claims—A Comprehensive Review, *Critical Reviews in Food Science and Nutrition*, 55:7, 919-929, DOI: [10.1080/10408398.2012.657809](https://doi.org/10.1080/10408398.2012.657809)

To link to this article: <https://doi.org/10.1080/10408398.2012.657809>



Accepted author version posted online: 24 Aug 2013.
Published online: 24 Aug 2013.



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Tomato (*Solanum lycopersicum*) Carotenoids and Lycopenes Chemistry; Metabolism, Absorption, Nutrition, and Allied Health Claims—A Comprehensive Review

RASHIDA PERVEEN, HAFIZ ANSAR RASUL SULERIA, FAQIR MUHAMMAD ANJUM, MASOOD SADIQ BUTT, IMRAN PASHA, and SARFRAZ AHMAD

National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan

Tomato (Solanum lycopersicum) is one of the most essential herbaceous plants that have been probed against various life sight related disorders owing to array of phytochemicals. It is important source of vitamin C, potassium, folic acid, and carotenoids, such as lycopene. Carotenoids are the pigments synthesized during fruit ripening and responsible for the final red color of the tomato. Consumption of tomato and tomato-based products contribute to the absorption of carotenoids and lycopenes in human serum. Lycopene is chemically acyclic carotene with 11 conjugated double bonds, normally in trans configuration while isomerization occur in blood plasma for its better absorption. It has ability for adenosine deaminase inhibition that plays important role in the regression of tumor. Tomato also contain other active compounds, namely, neoxanthin, lutein, α -cryptoxanthin, α -carotene, β -carotene, cyclolycopene, and β -carotene 5, 6-epoxide. These components provide synergistic effect against various threats but still need further attention of the researchers. Both in vitro and in vivo studies have elucidated the potential of tomato against variety of metabolic syndromes. Latest research highlights the relationship between consuming tomato and its products with reduced risk of various maladies like obesity, hyperglycemic and hypercholesterolemic attributes, cardiovascular disorders, and cancer insurgences. Moreover, tomato and its bioactive components hold potential to become effective modules in diet-based regimens; however, integrated research and meta-analysis are still required to enhance meticulousness.

Keywords Tomato, carotenoids, lycopenes, functional food, metabolism and absorption, nutritional and health benefits

BACKGROUND

Fruits and vegetables are gaining immense importance in the domain of nutrition owing to presence of vital phytochemicals and bioactive molecules. Their health promoting potentials are due to presence of functional ingredients, e.g., polyphenols, flavonoids, tannins, anthocyanins, etc. (Butt et al., 2008). These compounds trigger and alter body metabolism and modulate detoxification mechanism. Thereby, provide protection against lifestyle disorders, cancer insurgence, etc. Nevertheless, antiox-

idant potential of fruits and vegetables varies thus their balanced consumption is better than reliance on few specific groups (Manach et al., 2004).

In this context, functional and nutraceutical foods have shared the disease load of huge population. This has led to the consumption of plant-based phytonutrients as preventives agents as dietary supplements. Recently, plant-based products such as tomato, onion, garlic, ginger, green tea, black cumin, and agro industrial byproducts, like citrus peel, rice bran, etc. have been considered as potential exploitable sources for functional food development. These are similar in appearance to conventional foods and used in normal diet but have advantages of aiding physiological functions. In essence, combination of functional foods and healthy life style has a positive contribution to health and well-being (Frereid et al., 2007).

Address correspondence to Rashida Perveen, PhD Scholar, National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan. E-mail: sarfraz.ahmad@uaf.edu.pk

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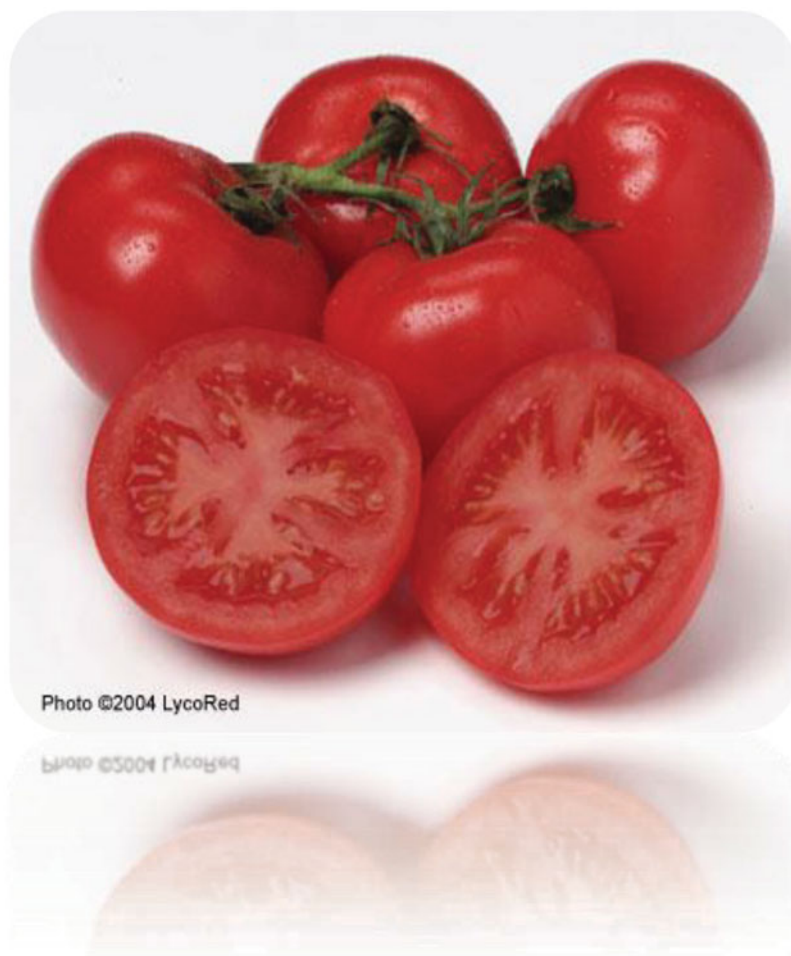


Figure 1 Tomato (*Solanum lycopersicum*).

Tomatoes are an integral part of diet worldwide, accounting lycopene in American diet, and also important component of the Mediterranean diet. Population studies have established a link between dietary intake of tomatoes having carotenoid and lycopene compounds that can reduce risk of various maladies, like cancer and cardiovascular diseases. The fruits of *Lycopersicum esculentum* have deep red color owing to carotenoid pigment that are synthesized during fruit ripening (Zeb and Mehmood, 2004). The fruits of *Lycopersicum esculentum* have deep red color owing to carotenoid pigment that are synthesized during fruit ripening (Fig. 1).

Phytochemicals are nonnutritive plant chemicals that have protective or disease preventive properties. They are nonessential nutrients and are not required by the human body for sustaining life. Among plant materials, fruits and vegetables contain phenolics, mainly belonging to the flavonoids family. Phenolic acids are different from other phenolic compounds by bearing acidic properties due to the presence of a carboxylic acid group (Liyana-pathirana and Shahidi, 2004). Foods containing phytochemicals are already part of our daily diet. In this context, tomato and tomato product contains lycopene, neoxanthin, violaxanthin, α -cryptoxanthin, zeaxanthin,

lutein, β -cryptoxanthin, β -carotene, g-carotene, z-carotene, α -carotene, phytoene, phytofluene, cyclolycopene neurosporene, and β -carotene 5, 6-epoxide (Fraser et al., 1994; Paetau et al., 1998; Khachik et al., 2002; Burns et al., 2003). α -carotene, β -carotene, and β cryptoxanthin have provitamin A activity, since they have been able in conversion of retinal in mammals (Burns et al., 2003). Chemical structures of different active components other than carotenoids in tomato have been shown in Fig. 2.

Tomatoes are mainly used as fresh commodity or in various processed form. Canned and sun-dried tomatoes, ketchup, pastes, juices, purees, soups, sauces, and salads are important processed tomato products (Shi and Le Maguer, 2000). Comparatively, the activity of antioxidants of commercial processed tomato products is limited owing to lycopene content (Willcox et al., 2003). Reactive oxygen species (ROS) could be important causative agents in number of human diseases, including coronary heart disease (CHD), and cancer insurgence. So the high intake of particular fruits and vegetables, which are the main sources of antioxidants, is suggested resulting decrease of the potential stress of various threats (Pellegrini et al., 2000).

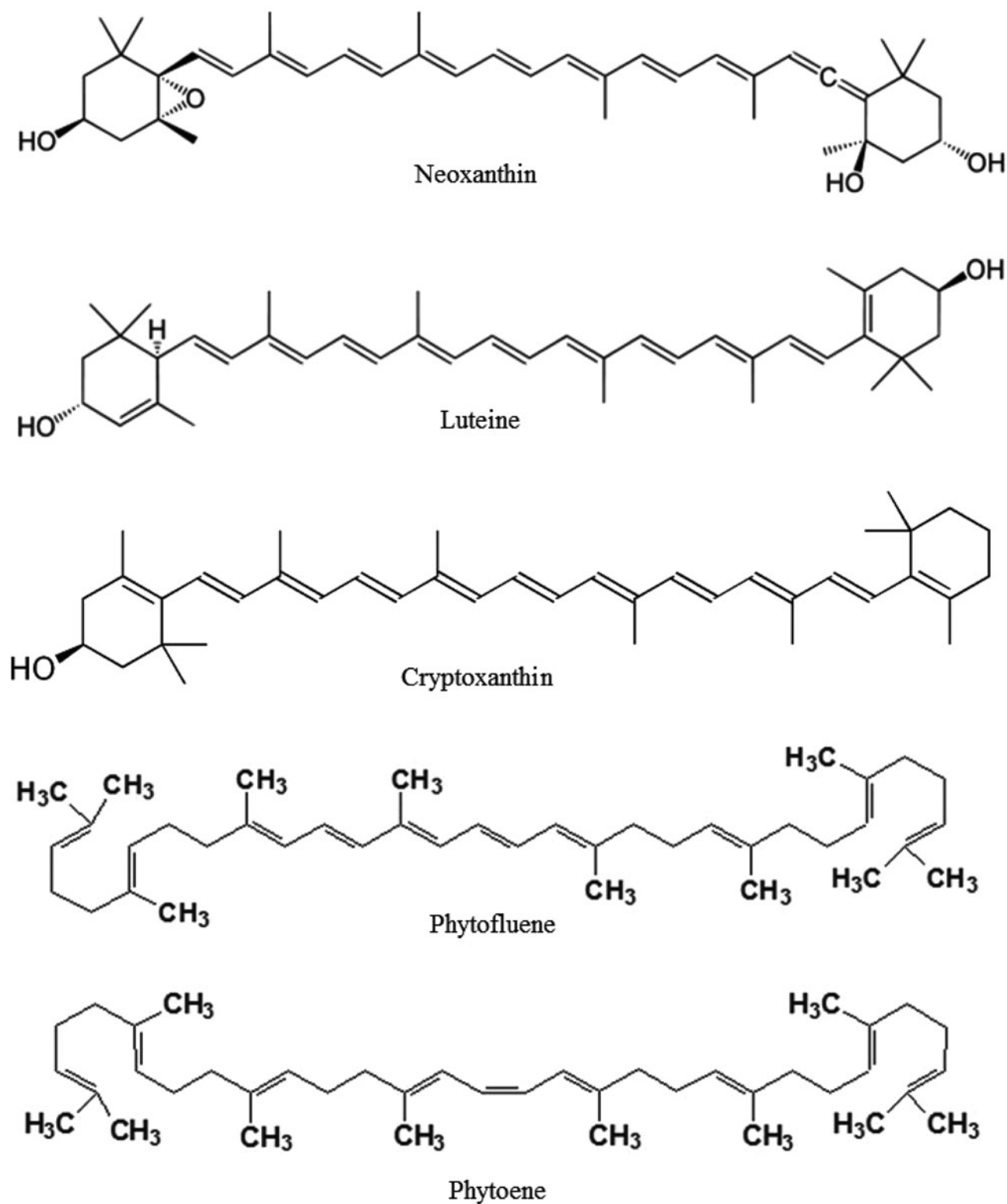


Figure 2 Different active components in tomato and their chemical structure.

Many epidemiological studies have shown the importance of fruits and vegetables in the human diet in the prevention of different diseases but recently, particular attention has been devoted to tomato and its products (Frusciante et al., 2000). Giovan-

nucchi et al. (1995) and Franceschi et al. (1994) reported that the consumption of tomato and its various products like sauces, pizza, and ketchup could inversely correlated with the risk of tumors in the digestive tract and the prostate. Experimental studies

reported that lycopene is an excellent antioxidant that can protect various cancerous cells (Carputo et al., 1999; La Vecchia, 2002).

TOMATO PLANT OVERVIEW

Tomato (*Solanum lycopersicum*) typically red fruit belongs to the nightshade family having 1–3 meters (3–10 ft) in height with weak stem that often sprawls over the ground and may vines over other plants. It is perennial plant often grow outdoors in temperate climates. The tomato fruit is consumed in diverse ways, including raw, as an ingredient in many dishes and sauces, and in drinks. It is botanically a fruit and only considered as vegetable during culinary purposes that cause some confusion. The fruit is rich in lycopene, which may have beneficial health effects. Tomatoes and tomato-based food products are the major source of lycopene and a number of other carotenoids, such as phytoene, phytofluene, α -carotene, β -carotene, gamma-carotene, and neurosporene. While tomato-based products are reported to be the primary source of dietary lycopene in the United States. Over the past decade, there has been increased interest in the health benefits of lycopene consumption (Story et al., 2010). Chemical structures of different carotenoids in tomatoes have been shown in Fig. 3.

STRUCTURE AND FORMATION OF CAROTENE

Lycopene is defined chemically as an acyclic carotene with 11 conjugated double bonds, normally present in the all-trans configuration. The double bonds are subject to isomerization, and various cis isomers are found in plants and also in blood plasma. Since the human body is unable to synthesize carotenoids endogenously so the body is totally dependent on dietary source carotenoids. In general, 85% of dietary lycopene in human diet is coming from tomato fruit and tomato-based food products (Handely et al., 2002; Walfisch et al., 2003).

Carotenoids like lycopene are important pigments found in plants, photosynthetic bacteria, fungi, and algae. They are responsible for the bright colors of fruits and vegetables and protection of photosynthetic organisms from excessive light damage. Lycopene is a key intermediate in the biosynthesis of many important carotenoids, such as β carotene, and xanthophylls. Formation of β carotene begins with mevalonic acid conversion into dimethylallyl pyrophosphate followed by condensation with three molecules of isopentenyl pyrophosphate and to give geranylgeranyl pyrophosphate. Moreover, two molecules of this product further condensed tail-to-tail to give 40 carbon phytoene. Through several desaturation steps, phytoene is converted into lycopene and then two terminal isoprene groups can be cyclized to produce β carotene that can then be transformed into a wide variety of xanthophylls (Armstrong and Hearst,

Table 1 Nutritional profile of tomatoes

Nutrient	Value per 100 g
Water	94.78
Protein	1.167
Total lipids	0.19
carbohydrate	3.18
Minerals mg/100 g	
Calcium (Ca)	5
Magnesium (Mg)	8
Phosphorus (P)	29
Potassium (K)	212
Sodium (Na)	42
Zinc(Zn)	0.14
Manganese (Mn)	0.088
Total dietary	0.9
Vitamins mg/100 g	
Vitamin C, total ascorbic acid	16
Thiamin	0.046
Riboflavin	0.034
Niacin	0.059
Pantothenic acid	0.018
Vitamin B-6	0.06

1996). An illustration of the formation of β -carotene has been given in the Fig. 4.

Tomatoes provide for each of the nutrients of which it is a good, very good, or excellent source. It contains high moisture, protein, total lipids, and carbohydrates 94.78%, 1.167%, 0.97%, and 3.18%, respectively. Considering minerals tomato contains such as calcium (Ca), magnesium (Mg), phosphorus (P), and others along with total dietary fiber. Tomato contain high amount of vitamin C showing best source of this vitamin and considered reasonable source for human nutrition. Consumption of different varieties of tomatoes like Lido, Raf. Rambo, Pera, or Racimo could provide a sufficient amount of vitamin C to meet the recommended daily allowance of 60 mg per person per day. It also has strong profile of thiamine, riboflavin, niacin, pantothenic acid, and vitamin B6.

Tomato also contains trace amount of saturated, polyunsaturated fatty acids, and free cholesterols which help to prevent many heart diseases. Lavelli et al. (2000) reported that tomato pulp contains some essential amino acids while its seeds have higher amounts of minerals (Fe, Mn, Zn, and Cu). They also have monounsaturated fatty acids especially oleic acid and linolenic acid. Aspartic acid, glutamic acid have highest amount present in tomato 0.16 and 0.42 mg, respectively, mentioned in Table 2.

CHEMISTRY AND METABOLISM OF CAROTENOIDS

Once lycopene 5, 6-epoxide is formed, it can rearrange to 2, 6-cyclolycopene-1, 5-epoxides A and B in acidic condition, this reaction may also be catalyzed by certain enzymes in human physiological system. Conversion of lycopene 5, 6-epoxide to 2, 6-cyclolycopene-1, 5-epoxides A and B followed by hydrolysis to their corresponding diols may be nonenzymatic and take place

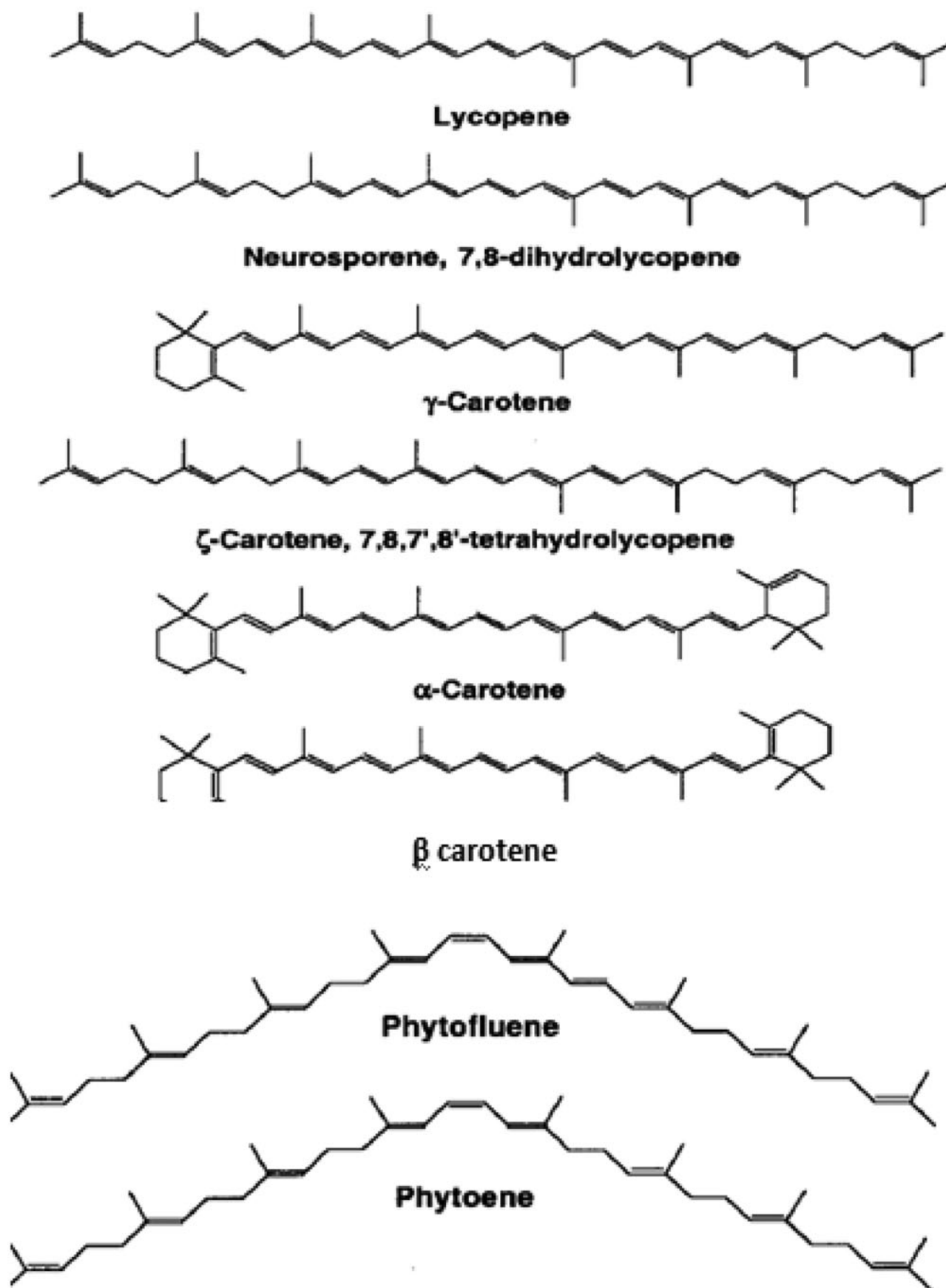


Figure 3 Chemical structure of carotenoids in tomatoes.

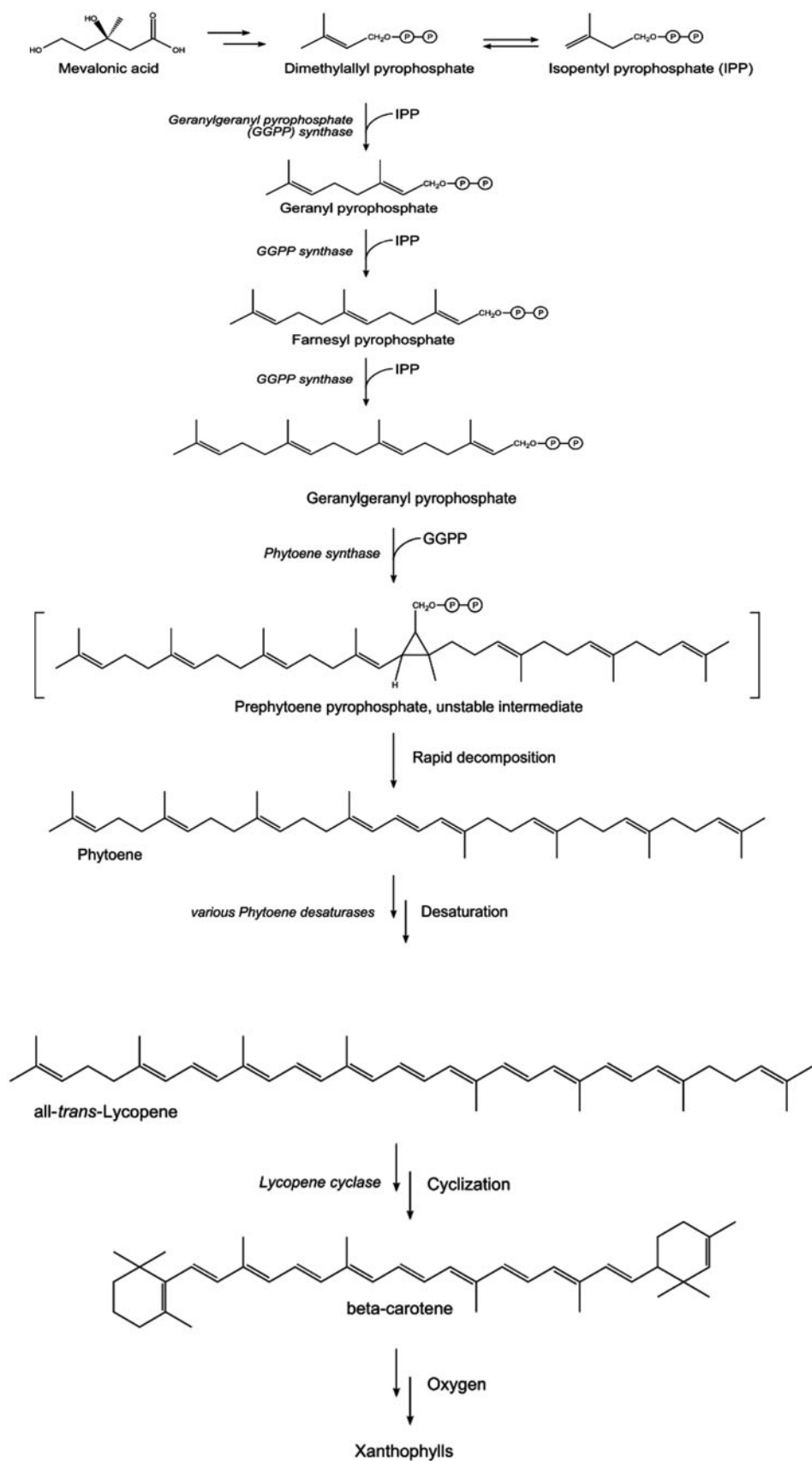


Figure 4 Formation of β -carotene.

Table 2 Amino acids and fatty acids profile of tomatoes fruit

Tryptophan	0.008
Threonine	0.029
Isoleucine	0.027
Leucine	0.042
Lysine	0.042
Methionine	0.010
Cystine	0.015
Phenylalanine	0.030
Tyrosine	0.020
Valine	0.030
Arginine	0.029
Histidine	0.018
Alanine	0.033
Aspartic acid	0.161
Serine	0.031
Fatty acid total saturated	0.025
4:0	0.00
16:0	0.019
18:0	0.007
Fatty acid monosaturated	0.028
Fatty acid polyunsaturated	0.076
Cholestrol	0
Phytosterol	4

in human stomach owing to acidic condition. Unfortunately, the fact that 2, 6-cyclolycopene-1, 5-diols A and B and their precursors 2, 6-cyclolycopene-1, and 5-epoxides A and B are also found in tomato products at low concentrations makes it difficult to differentiate between the various processes which may ultimately responsible for the presence of these compounds in human serum and tissues as described in Fig. 5 (Khachik et al., 2002). Metabolic and absorptive pathway of lycopene in tomatoes is given in the Fig. 5.

Tomatoes that are the major source of carotenoids like α -carotene, β -carotene, and ∞ -carotene consider as precursors of vitamin A. In general, tomato and tomato-based products provide at least 85% of dietary lycopene in humans. The remaining 15% are usually obtained from watermelon, pink grapefruit, guava, and papaya, although at much lower levels than tomatoes. Concentrations of these carotenoids in tomatoes and tomato based food products are given in the Table 3.

Fruits and vegetables contain more than 40 carotenoids that are routinely absorbed and metabolized by human body. Intake of tomato and tomato-based products contributes to the absorption of a wide range of carotenoids in human serum and tissues.

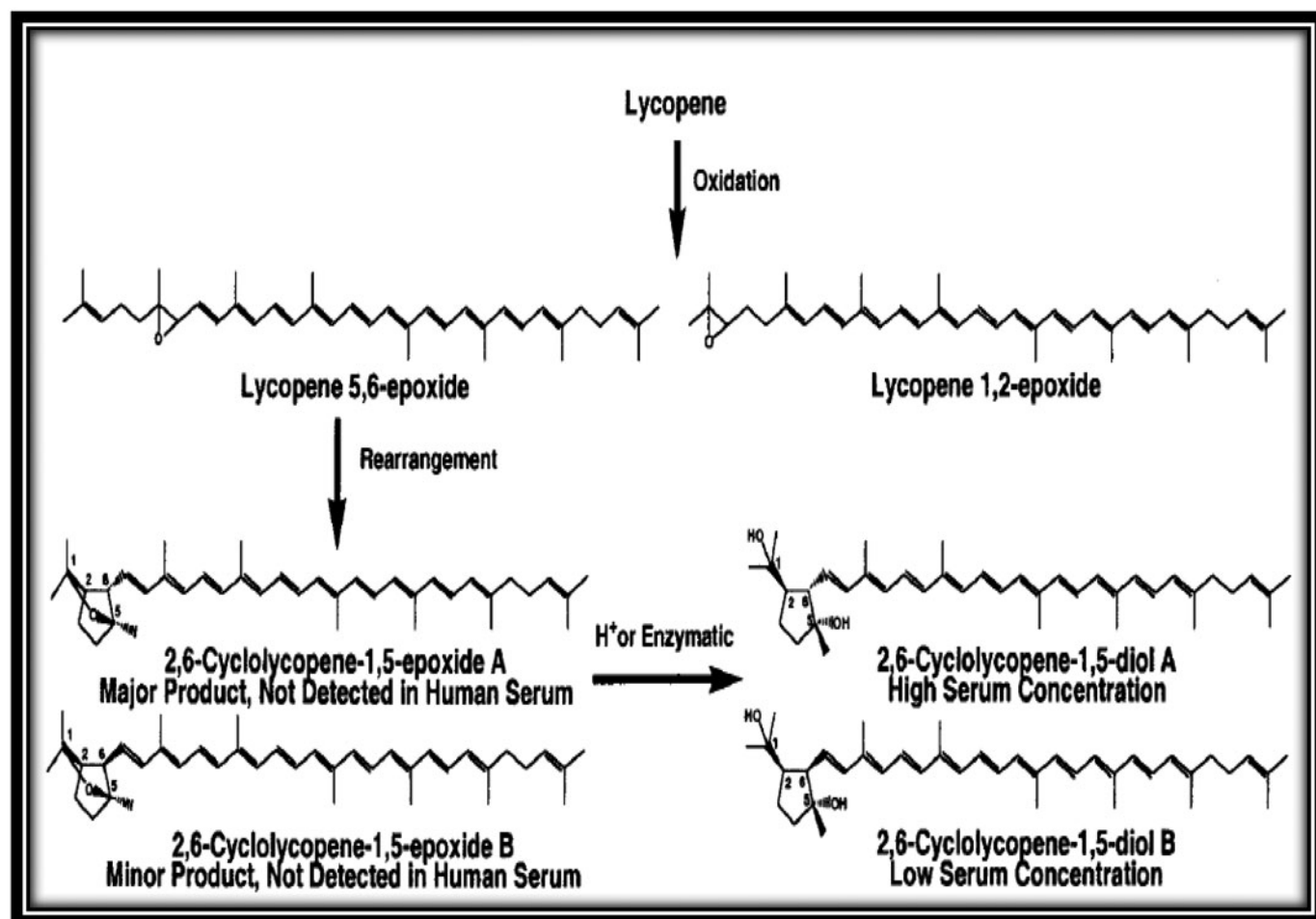
**Figure 5** Metabolic and absorptive pathway of tomatoes.

Table 3 Concentration of carotenoids in tomatoes and tomato-based food products (mg/100 g)

Foods	Lycopene	Neurosporene	Phytofluene	Phytoene	Lutein	β -Carotene	∞ -Carotene
Raw tomato	9.25	1.18	0.80	1.86	0.07	0.41	0.00
Tomato paste	55.43	6.94	3.63	8.36	0.34	1.27	9.95
Tomato sauce	17.96	2.45	1.27	2.95	Traces	0.45	3.37
Tomato puree	16.60	2.60	1.07	2.38	0.08	0.58	3.03
Tomato juice	10.76	2.05	0.81	2.77	0.05	0.43	1.07

MEDICINAL PERSPECTIVES

Bad Cholesterol Reduction

Tomato contain active ingredient called as “tomatine” that has a strong affinity for reducing cholesterol level *in vitro* and *in vivo*. Some studies showing tomatoes role in disease prevention are given in the Table 5. It was investigated by Friedman et al. (1996) that this does not appear to be toxic when consumed orally by rats ($LD_{50} = 900\text{--}1000$ mg/kg body weight). According to one another study of Mendel et al. (2000) diet containing a high concentration of tomatine (0.2%) was fed to hamsters along control group. The diet containing an active ingredient tomatine decreased LDL cholesterol by 41% while did not change HDL cholesterol level (Mendel et al., 2000). Several lines of evidence suggest that oxidative LDL damage arterial walls result in atherosclerosis.

Fuhrman et al. (1997) reported that utilization of tomato lycopene, alone or in combination with other natural antioxidants, inhibits LDL oxidation. Moreover, dietary supplementation of tomato's lycopene (60 mg/day) for a three-month period resulted in a significant reduction in plasma LDL cholesterol. Animal feeding the tomatine diets has reduced the plasma LDL cholesterol with increasing dietary tomatine content. This increase in trend of cholesterol and ratio of coprostanol to sitostanol is also consistent with increasing binding of cholesterol due to increase of tomatine concentrations (Mendel et al., 2000).

Obesity

Finucane et al. (2011) revealed that rapid increase in obesity with an estimated 1.46 billion adults worldwide now classified

as overweight ($BMI > 25$ kg/m²). It is a major risk factor for the development of other chronic diseases like cardiovascular disease, liver damage, and cancer insurgence (Calle et al., 1999; Cummings and Schwartz, 2003). High consumption of both a high-fat diet (HFD) and alcohol further increases risk of cardiovascular and liver disease.

It was reported by A-Young et al. (2012) that functional effects of tomato-wine with supplementation of lycopene content on HFD-fed rats. Fifty male Sprague–Dawley rats were divided into five groups and fed a HFD (35% kcal fat) with ethanol (7.2% kcal alcohol) along with tomato-wine with lycopene content (0.425, 1.140, or 2.045 mg, respectively) or an isocaloric control diet for six weeks. It was reported that tomato-wine extract enriched with lycopene content suppressed gain in body weight. Supplementation of tomato-wine containing lycopene suppressed more body weight gain over six weeks in HFD fed rats compared to both ethanol/HFD fed rats and pair-fed controls. However, there were no dose-dependent effects of lycopene content on body weight gain. These results suggest the low dose of lycopene contained in the tomato-wine was sufficient to suppress body weight gain. Other studies on tomato-based products containing lycopene have reported no effect on body weight gain (Hsu et al., 2008; Ibrahim et al., 2008; Veeramachaneni et al., 2008), which may be due to methodological differences between studies such as tomato

Table 5 Overview of disease prevention by tomato

Disease	Authors	Model
CVD	Lindshield et al. 2007	Rat study
	Sesso et al. 2003	Human study
	Alshatwi et al. 2010	Human case control study
Type 2 diabetes	Story et al. 2010	Rat study
Oral drug	Naisbett and woodly, 1995	Rat study
Prostate cancer	Giovannucci et al. 2002	Human case control study
	Etminan et al. 2004	Human study
	Giovannucci et al. 1995	Human case control study
Breast cancer	Kucuk et al. 2001	Human case study
Lung and stomach cancer	Giovannucci, 1999	Human study
CHD	Rissanen et al. 2003	Rat study
	Sesso et al. 2004	Rat study
	Klipstein-Grobush et al. 2000	Human case study

Table 4 Lycopene content in different fruits

Food type	Amount mg per 100 g	References
Guava fresh, pink	5.4	USDA, 1998
Tomatoes fresh, red	3.1–7.7	Nguyen and Schwartz, 1998
Tomato juice	7.83	Nguyen and Schwartz, 1998
Tomato paste	30.07	Nguyen and Schwartz, 1998
Grapefruit fresh, pink	3.36	Nguyen and Schwartz, 1998
Watermelon fresh, red	4.1	USDA, 1998
Ketchup	16.6	USDA, 1998
Pizza sauce	32.9	Nguyen and Schwartz, 1998
Spaghetti sauce	17.5	Hadley et al., 2002
Papaya fresh, red	2.0–5.3	Mangels et al., 1993

processing, diet composition, duration of diet, and experimental animals used (Kim et al., 2008).

Markovits et al. (2009) revealed that a recent small-scale clinical trial showed that lycopene did not increase weight-loss in obese humans, but these findings may have been due to several factors including the intervention duration, dietary intake, lycopene dose, or the small sample size. No previous studies have reported tomato wine can suppress body weight gain in mammals fed a HFD. Tomato-wine with high lycopene content appeared to be the most effective at suppressing in total white adipose tissue in HFD fed rats. Liver weight increases in HFD fed rats is an indicator of fatty liver and hepatosis development. Morphological analysis of liver indicated lipid accumulation was most pronounced in the ethanol/HFD fed rats compared to pair-fed controls.

Oxidative Stress

The process of oxidation is essential in vitality of life coupled with production of ROS. A natural balance between ROS production and antioxidant defense system exist and its imbalance results in oxidative stress resulting in damage to membranes and cell constituents such as DNA, lipids, and proteins. The intake of antioxidant rich diets or supplementation with bioactive molecules, like vitamins, carotenoids, and tannins may provide protection against oxidative damage (Ahn et al., 2002; Madhujith et al., 2006; Lee et al., 2006; Gu et al., 2008).

Lindshield et al. (2007) have demonstrated that lycopene has antioxidative perspectives, which can prevent DNA damage and hence protect against mutations that cause cells cancer development. Furthermore, recent studies reflect that lycopene may also modify molecular biomarkers of atherosclerosis (Hsu et al., 2008; Ibrahim et al., 2008; Badimon et al., 2010) while studies on the dose-dependent effects of lycopene have reported conflicting results. For instance, higher lycopene intake (20 mg lycopene/kg diet) from tomato paste was reported to improve plasma lipid profiles in rodent experimental modeling (Ibrahim et al., 2008). There have been several studies showing tomato processing affects the lycopene content (Story et al., 2010). Moreover, dietary factors and processing are reported to modulate the bioavailability of lycopene (Agarwal et al., 2001; Story et al., 2010). Hence, there is scope for the development of novel dietary supplements to maximize the bioavailability of phytochemicals such as lycopene while also seeking to understand its functional role in health and disease.

Coronary Heart Diseases

Coronary heart disease (CHD) is one of the primary causes of death in the Western world. The emphasis of research so far has been on the relationship between serum cholesterol levels and the risk of CHD. In the industrialized world, cardiovascular disorders (CVD) are responsible for one of every three deaths in

both men and women. Gorinstein et al. (1994) considered higher level of total cholesterol, LDL cholesterol (LDL-C), triglycerides, apolipoproteins B and C-III, and a reduced level of high density lipoprotein cholesterol (HDL-C), and apolipoproteins A-I as major risk factors (Gorinstein et al., 1998). Oxidation of LDL-C particles (Witztum and Steinberg, 1991; Aviram, 1993) results in accumulation of lipids into arterial wall resulting in onset of atherosclerosis (Steinbrecher et al., 1990; Gorinstein et al., 2000). Diets especially fruits and vegetables are the natural sources of nutritional antioxidants thus preventing LDL oxidation (Hertog et al., 1995; Kromhout et al., 2002; Park et al., 2006).

The evidence in support of the role of lycopene in the prevention of CHD is based on epidemiological observations of normal and at-risk populations. The most impressive population-based evidence comes from a multi-center case-control study (the EURAMIC study). According to this study, subjects from 10 European countries were evaluated for a relationship between their antioxidant status and acute myocardial infarctions. By providing different dietary variables, only lycopene levels were found to be protective. These results were also confirmed by another Rotterdam Study (Klipstein-Grobusch et al., 2000).

Serum lycopene concentration plays a vital role in the early stages of atherosclerosis. Increased thickness of intima-media (the innermost lining of a blood vessel) has been shown to predict coronary events. A low serum lycopene concentration in Eastern Finland associated with an increased thickness of the intima-media. Recently, a prospective case-control study was conducted by Harvard University researchers on 39,876 women. According to them higher plasma lycopene concentrations are associated with a lower risk of cardiovascular disease in middle-aged and elderly women. Moreover, the possible inverse associations with cardiovascular disease for higher levels of tomato-based products suggest that dietary lycopene or other phytochemicals consumed as oil-based or oil-containing tomato products confer cardiovascular benefits (Sesso et al., 2004; Rissanen et al., 2003).

Cancer Insurgence

Sengupta et al. (2002) suggested that the consumption of garlic and tomato can reduce the damaging effect of carcinogenic. They also reported that different constituents of garlic and tomato can be protected chromosomal aberrations especially lycopene have ability to protect the cell against oxidative damage. So tomato and tomato products not only reduce the risk of cardiovascular diseases but also cure cancer insurgence (Alshatwi et al., 2010).

Epidemiology data indicated that reduction of prostate cancer in men was observed those who consume tomato and tomato-based products. In the Health Professionals Follow-Up Study, intake tomato products in week resulted in a lower risk of prostate cancer (Giovannucci 2002). It also has been reported that intake of tomato compound may lower down prostate

cancer while carotenoids fraction are not related to prostate risk (Ziegler, 1991; Giovannucci et al., 1995). Lycopene is dominant antioxidant has been found to be very active in suppressing the certain cancer cell in humans. Lycopene causes an increase in intercellular communications, increased differential, and change the phosphorylation of regulatory proteins and act as antitumorigenic effect (Bankson et al., 1991; Zhang et al., 1992; Durak et al., 2003; Matsushima et al., 1995). A comprehensive review of the epidemiological literature on the relation of tomato consumption and cancer was published by Giovannucci (1999). He found that among 72 studies, 57 reported inverse associations between tomato intake or blood lycopene level and the risk of cancer at a defined anatomic site. Thirty-five out of 57 of these inverse associations were statistically significant. A recently published meta-analysis by Etminan et al. (2004) formulated the assumption that intake of tomato-based products reduces the risk of prostate cancer. It was also observed that the prevention was slightly stronger for high intakes of cooked tomato products than raw tomatoes due to the bioavailability of lycopene, which is increased with processing, heat, and presence of fat.

CONCLUSION

Fruits and vegetables are gaining immense importance in the domain of nutrition owing to presence of vital phytochemicals and bioactive molecules. Their health promoting potentials are due to presence of functional ingredients, e.g., polyphenols, flavonoids, tannins, and anthocyanins. These compounds trigger and alter body metabolism and modulate detoxification mechanism. Thereby, provide protection against lifestyle disorders and cancer insurgence. Concluded that moderate amounts of whole food-based supplementation (2–4 servings) of tomato soup, tomato puree, tomato paste, tomato juice, or other tomato beverages, consumed with dietary fats, such as olive oil or avocados, leads to increases in plasma carotenoids, particularly lycopene. These foods may have both chemopreventive as well as chemotherapeutic values. In the light of recent clinical trials, a combination of naturally occurring carotenoids, including lycopene, in food sources and supplements, is a better approach to disease prevention and therapy, versus a single nutrient. However, until further research establishes significant health benefits of lycopene supplementation in humans, the conclusion may be drawn that consumption of naturally occurring carotenoid-rich fruits and vegetables, particularly processed tomato products containing lycopene, should be encouraged, with positive implications in health and disease.

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