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Tomato lycopene: Potential health benefits

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Abstract
Lycopene is a member of carotenoid family and a lipid soluble antioxidant synthesized by many plants and microorganisms but not by animals and humans. It is a 40 carbon poly-isoprenoid compound containing 13 double bonds and is principally responsible for characteristic deep-red color of ripe tomato. Tomato and processed tomato products are the primary source of dietary lycopene. Lycopene is an essential nutrient for human and its consumption has been considered as a potential means for prevention of cancer, cardiovascular, diabetes etc. Tomato lycopene bioavailability is greatly affected by dietary composition and processing operations. Being a lipid-soluble compound, consuming lycopene with fat increases its bioavailability. Lycopene in fresh tomatoes mainly occurred as all *trans* form of isomer but geometrical isomerization during food processing converts all *trans* form to *cis* form which are better absorbed in human tissues. This review summarizes the current understanding of lycopene with respect to health benefits and prevention of various diseases.

Keywords: Lycopene, tomato, antioxidant, health benefits, cancer, cardiovascular disease

Introduction

Tomato (*Lycopersicum esculentum*) fruit is known for its distinctive pleasant flavour and nutritional goodness with respect to its antioxidant efficacy (Kong *et al*, 2010) [19]. Tomato contains all four major carotenoids: alpha and beta-carotene, lutein and lycopene (Mohammed and Malami, 2013) [22]. Lycopene is a bright red carotenoid pigment principally responsible for the deep-red color in many fruits and vegetables, but excessively found in tomatoes and tomato products (Gartner *et al*, 1997 and Kopec *et al.*, 2010) [19]. It is the potent antioxidant and primarily occurs in red tomatoes and processed tomato products including tomato juice, tomato sauce, tomato puree, ketchup and pizza sauce contributing 90% dietary share in human (Capanoglu *et al*., 2010 and Story *et al.*, 2010) [8]. Among the carotenoids with potentially beneficial biological activities, recently lycopene has received significant attention on the basis of its role in reduction of cancer risk and other non-communicable diseases (Fiedor and Barda, 2014). Tomato lycopene exhibits the highest antioxidant activity and singlet oxygen quenching ability of all dietary carotenoids (Alda *et al*., 2009 and Chun *et al.*, 2009) [19]. Lycopene quenches free radical and delays or inhibits cellular damage (Ganesh *et al*., 2016) [15]. Epidemiological studies on lycopene and non-communicable diseases have correlated increased tomato intake with lower incidence of gastrointestinal, stomach, and prostate cancers while decreasing serum values of lycopene increases the risks for various non-communicable diseases (Mohammed and Malami, 2013) [22]

Lycopene is a member of carotenoid family and a lipid soluble antioxidant synthesized by many plants and microorganisms but not by animals and humans (Chauhan *et al.*, 2011) [11] [11].Tomato and processed tomato products constitute the major sources and reports for more than 85% of all the dietary sources of lycopene. The lycopene content in tomato differs with variety and increases as the fruit ripens (Alda *et al.*, 2009) [2]. Lycopene content in fresh tomato varies from 0.85mg to 13.6 mg/ 100g (Chauhan *et al.*, 2011) [11] and lower lycopene levels are found in peeled tomatoes as the removed peel is recognized to have higher content (Nguyen and Schwartz, 1998) [23].

Lycopene is a 40 carbon poly-isoprenoid compound containing 13 double bonds (Kong *et al.*, 2010) [19]. It is a lipid soluble carotenoid, sensitive to oxidation and its degradation during processing is dependent on temperature, light, acidity and oxygen (Alda *et al.*, 2009 and Xianquan *et al.*, 2005) [32]. Thus it is susceptible to loss of provitamin A activity through oxidation during processing (Kong *et al.*, 2010) [19].

The consumption of tomato and tomato products containing lycopene has been shown to be associated with decreased risk of chronic diseases such as cancer and cardiovascular diseases

In several epidemiological studies (Agarwal *et al.,* 2000) [1]. The health benefits of lycopene are mainly attributed to its antioxidant properties (Alda *et al*., 2009) [2]. Lycopene quenches singlet oxygen almost twice as well as carotene (Shi *et al.,* 2000) [28].

Structure of Lycopene

Lycopene is a lipophilic red-colored carotenoid pigment, composed of eight isoprene units (octaprene) joined by regular head to tail bindings, except in the middle of the molecule where the binding is tail to tail, giving rise to a symmetric structure. Lycopene is insoluble in water, almost insoluble in methanol and ethanol, and soluble in organic solvents such as carbon disulphide, ethyl ether, petroleum ether, chloroform, and benzene (Camara *et al.,* 2013 and Chauhan *et al.*, 2011) [11].

The chemical formula for lycopene is $C_{40}H_{56}$. Lycopene is a highly unsaturated with 40 carbon acyclic molecule containing 11 conjugated and 2 unconjugated double bonds arranged in all trans configuration in tomatoes. The seven double bonds can isomerize to form mono- orpoly-*cis* isomers upon exposure to heat, light, and certain chemical reactions or during processing or storage (Shi *et al*., 2000) [28]. Interestingly, *cis*-isomers account for over 50% of the total lycopene in human serum and over 80% in tissues such as prostate (Allen *et al.,* 2002) [3]. Thermodynamic stability study of the common lycopene isomers reported 5-cis lycopene as the most stable isomer followed by all trans, 9 cis, 13 cis, 15 cis, 7 cis and 11 cis and with highest antioxidant properties followed by 9 cis,7 cis, 13 cis, 11 cis and all trans isomer (Chasse *et al.,* 2001) [9]. The color of lycopene is directly related to its isomeric form. The all-*trans* isomer and most other isomers of lycopene are red, whereas tetra-*cis*-lycopene possesses an orange hue (Nguyen and Schwartz, 2000). Lycopene degradation take place with light, heat, oxygen, metallic ions of copper and iron catalyzing oxidation and acids (Chauhan *et al,*. 2011) [11].

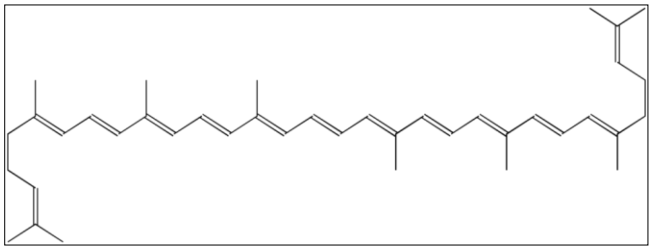

Fig 1: Molecular structure of all *trans* form of lycopene isomer (Camara *et al.,* 2013) [7]

Lycopene bioavailability

The bioavailability of lycopene is predominantly affected by processing technology. It is more with cooked or processed tomato products (Alda *et al*., 2009) [2]. Lycopene is bio synthesized in plants mainly as the all- *Trans* isomer (Kong *et al.,* 2010) [19]. Most available sources of lycopene maintain the natural isomeric distribution ratio. During food processing lycopene undergoes geometrical isomerisation, increasing the proportion of *cis* isomers (Alda *et al*., 2009) [2]. Lycopene may isomerize to *cis*-forms in presence of heat (Xianquan *et al*., 2005) [32]. *Cis* isomers of lycopene are better absorbed than the all-*trans* form (Alda *et al.,* 2009) [2].

The amount of lycopene present in processed tomato products is often much higher in fresh tomatoes given that processing often involves concentrations via water loss. Multiple studies have shown that lycopene from thermally processed tomato products was more bioavailable than lycopene from fresh tomatoes (Gartner *et al.,* 1997) [16].

Absorption of lycopene is similar to other lipid soluble compounds and is absorbed across gastro intestinal tract via a chylomicron mediated mechanism and is released into lymphatic system for transport to the liver (Gartner *et al.,* 1997) [16]. It accumulates in hepatocytes and to a lesser extent in spleen (Rao *et al.,* 2002). In general 10-30% of dietary lycopene is absorbed by human and is equally absorbed from different sources of lycopene including tomato sauce, juice or tomato oleoresin capsule (Gartner *et al.,* 1997 and Rao *et al.,* 2002) [26]. However, its absorption is affected by several factors containing the breakup of food matrix, cooking temperature, presence of lipids, dosage and other soluble compounds including the other carotenoids. These factors cause the free of lycopene from the food matrix and thus increase its bioavailability. The bioavailability of lycopene was less in those 60–75 years of age compared to those 20–35 (Porrini *et al.,* 1998 and Grolier *et al*., 2000) [18].

Lycopene bioavailability can be affected by a number of factors, including food processing and dietary composition. Lycopene can occur in several forms in fresh plant foods, including carotenoid-protein complexes in chloroplasts or in crystalline form inside chromoplasts (Story *et al.,* 2010) [30]. Lycopene bioavailability in processed tomato products is higher than in unprocessed fresh tomatoes (Camara *et al.,* 2013) [7]. Food processing results in increased lycopene bioavailability by breaking down cell walls that weakens the bonding forces between lycopene and tissue matrix, thus making lycopene more accessible (Alda *et al.,* 2009) [2]. Exposure to light and oxygen during improper processing and storage may alter the ratio of lycopene isomers or degrade lycopene entirely, making thesefood products less desirable to the consumer (Xianquan *et al.,* 2005) [32]. Lycopene bioavailability is greatly affected by dietary composition. Being a lipid-soluble compound, consuming lycopene with fat increases its bioavailability (Brown *et al.,* 2004) [6]. In human lycopene absorption is in the range of 10-30%, with the remainder being excreted (Rao and Agarwal, 1998) [27].

Health benefits of Lycopene

Lycopene being a predominant carotenoid in tomatoes, exhibits the highest antioxidant activity and singlet oxygen quenching ability of all dietary carotenoids. It is an essential nutrient for human and its consumption has been considered as a potential means for prevention of chronic diseases like cancer, cardiovascular, diabetes etc. (Alda *et al.,* 2009 and Camara *et al*., 2013) [7]. Free radical in human body can induce cell damage and consequently responsible for the development of some cancers and chronic diseases (Marques *et al.,* 2015) [21]. Several epidemiologic studies reported that lycopene enriched diet including tomatoes and tomato products protect against various chronic diseases by mitigating oxidative damage (Agarwal *et al.,* 2000, Kopec *et al.,* 2010 and Chauhan *et al*., 2011) [11].

Cardiovascular disease

Cardiovascular disease (CVD) affects the normal function of the cardiovascular system involving heart and blood vessels. Increased plasma lycopene levels have been associated with reductions in CVD risk and have also been reported to improve biomarkers associated with CVD (Kopec *et al.,* 2010 and Chauhan *et al.,* 2011) [11]. Low plasma lycopene levels

were reported by many researchers in hypertension, myocardial infarction, stroke, and atherosclerosis (Wolak *et al.,* 2013) [31]. Agarwal *et al.* (2000) [1] reported that lower blood lycopene levels are associated with increased risk for death from coronary artery disease. Lycopene may have a cholesterol synthesis-inhibiting effect and may enhance LDL degradation leading to prevention of cardiovascular diseases in humans (Arab *et al*., 2000).

In a epidemiologic study, 19 healthy subjects consumed placebo (0mg lycopene), tomato juice (50.4mg lycopene), spaghetti sauce (39.2mg lycopene), and tomato oleoresin (75mg lycopene) treatment daily for one week and went through a one-week washout period between each treatment week. The serum lycopene concentration doubled in subjects on lycopenecontaining treatments and also a significant decrease in serum lipid peroxidation and LDL oxidation was observed after subjects consumed any one of the three lycopene-containing treatments (Agarwal and Rao, 1998).Several clinical trials have proved that lycopene consumption can contribute to cancer and CVD treatment (Agarwal *et al.,* 2000, Chauhan *et al*., 2011 and Ganesh *et al.,* 2016) [15]**.** Lycopene may reduce cholesterol synthesis and increase low-density lipoprotein (LDL) degradation. Plasma low density lipoprotein (LDL) isthe major risk factor of CVD and is associated with increasing risk of atherosclerosis and coronary heart disease (Chauhan *et al.* 2011) [11].

Cancer

The consumption of lycopene as sole or in the form of tomatoes and tomato base products has been associated with a reduced incidence of different types of cancers, including prostate, breast, lung, stomach, cervical, ovarian, liverand other organ sites (Giovannucci, 1999 and Agarwal *et al.,* 2000) [1]. Anti-proliferative properties of lycopene are effective against the risk of prostate and other types of cancer Giovannucci (1999). Serum and tissue lycopene levels are inversely related to the incidence of several types of cancer, including breast cancer and prostate cancer Agarwal *et al.* (2000) [1]. Tomato lycopene is inversely associated with the risk of gastric cancer. Moreover high consumption of tomato and tomato products are related to approximately half the risk of oral cancer Giovannucci (1999) [14-17]. The diet rich in tomatoes and tomato based products with high lycopene content may help to reduce risk against cancers including pancreatic cancer (Marques *et al.,* 2015) [21].

Prostate cancer is the most common malignancy and cause of death in men. Although genetic factors and age are important determinants of the risk, environmental exposures, including diet are increasingly being associated with the disease (Chauhan *et al.,* 2011) [11]. The link between lycopene and the prevention of prostate cancer is supported by studies that have examined the plasma levels of lycopene in humans. Lycopene was the only antioxidant that occurred at significantly lower levels in men who went on to develop prostate cancer in comparison with status-matched controls (Gann *et al.,* 1999) [1].

Other diseases

There have been numerous other diseases that have also been investigated in relation to lycopene consumption including ultra violet (UV)-induced sunburn, gingivitis, osteoporosis, mental disorders, and asthma (Chandra *et al.,* 2007 and Camara *et al.,* 2013) [7]. The ability of lycopene to affect UV-induced sunburn was investigated and tomato paste treatment was found protective against UV-induced sunburn (Stahl *et al.,* 2001) [29]. A clinical investigation 36 healthy adults subjects were subjected to a treatment of synthetic lycopene alone, a soft-gel encapsulated tomato extract, or a tomato drink for 12 weeks. It was found that the subjects consuming the tomato extract and tomato drink had a 38% and 48% decrease, respectively, in solar simulator–induced sunburn at week 12, compared with only a 25% decrease in the group treated with synthetic lycopene (Aust *et al.,* 2005).

A randomized, placebo-controlled, split-mouth study of gingivitis was performed by Chandra *et al.* (2007) in 20 healthy subjects with clinical signs of gingivitis and this study indicates that patients receiving the lycopene treatmentshowed statistically significant reductions in gingivitis and bleeding index.

Oxidative stress as an important contributory factor in male infertility (Zini *et al.,* 1993) [34] Men with antibody-mediated infertility were found to have lower semen lycopene levels than fertile controls (Palan and Naz, 1996) [24]. Low serum levels of lycopene have also been associated with increased risk of psychiatric disorders (Zhang and Serum, 2007) [33].

Conclusion

Lycopene is an antioxidant carotenoid principally responsible for characteristic deep-red color of ripe tomato. It is the most predominant carotenoid in tomatoes exhibiting the highest antioxidant activity and singlet oxygen quenching ability of all dietary carotenoids. Lycopene as an essential nutrient for human and its consumption contributes to various health benefits including reducing risk of oxidative stress and chronic diseases like cancer, cardiovascular, diabetes etc. in human. Tomato lycopene bioavailability is greatly affected by dietary composition and processing operations. Lycopene in fresh tomatoes mainly occurred as all *trans* form of isomer but geometrical isomerization during food processing converts all *trans* form to *cis* form which are better absorbed in human tissues.

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