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REVIEW ARTICLE

Lycopene: A Natural Food Colorant Graduating to be a Potential Health Enhancer

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Abstract

Significance of lycopene - a phytochemical present in tomato and other foodstuffs of plant origin has evolved over the years, graduating from a natural food colorant to a potent antioxidant phytochemical with the realization that when free radicals accumulate beyond a *steady state of their generation and attenuation* in the human body, they snowball into oxidative stress to eventually become the means for causation of non communicable diseases (NCD's) such as cardiovascular and cancer. Antioxidants like lycopene act as antidotes to stem NCD's. There have been several studies that point towards inverse association between tomato intake or blood lycopene concentration and the risk of cancer and cardiovascular diseases. As a matter of fact, the role of lycopene in disease prevention and health promotion has become an active area of research in the contemporary times with lycopene being seen as one of the geroprotector phytochemicals; i.e. one of the substances whose consumption in diet on regular basis enhances life span as well as quality of life, adding not only years to life but also life to the years.

Keywords: Antioxidants, Free Radicals, Lycopene, Non Communicable Diseases (NCD's), Oxidative Stress.

Introduction

In addition to macronutrients, vitamins and other micronutrients necessary for the growth, maintenance and repair of body tissues, a plant based diet contains numerous components known as phytochemicals. The chemicals present in plants, though not required absolutely for basic body functions yet seemed consequential in health enhancement and disease mitigation. As a matter of fact, they are secondary plant metabolites which serve to protect the plant from external abiotic (heat, drought, excessive sunlight) and biotic (insects and animals) stress. Lycopene, a carotenoid other than those of vitamin A precursors acts as a potent antioxidant and richly present in tomatoes and other food stuffs of plant origin (*guava, watermelon, papaya, mango and carrots*) is gaining ground as an antidote ingredient of diet against the occurrence of NCD's.

In a happy augury to research endeavors in this area, phytochemicals present in plant based foodstuffs have begun to become the basis for food based strategies to prevent and manage NCD's. Among an array of phytochemicals explored and accredited, lycopene, a hitherto used food colorant has assumed an added importance as antioxidant. The present review focuses on lycopene chemistry and its role as a substance of neutraceutical nature by unraveling its efficacious streak in mitigating NCD's depredations.

As a matter of fact, sizeable lycopene consumption has been related to a lowered risk of cardiovascular other diseases, viz. atherosclerosis, myocardial infarction, stroke and cancer of prostate gland (Klipstein *et al.*, 2000; Rissanen *et al.*, 2001; Sesso *et al.*, 2004; Voutilainen *et al.*, 2006). Etiology of these diseases is related to oxidative stress, inflammatory processes, endothelial dysfunction and subsequent vascular remodelling. Several clinical trials have provided evidence that lycopene plays a pivotal role in lowering oxidative stress, Due to its chemical structure containing eleven conjugated double bonds, lycopene becomes powerful antioxidant and free radical quencher. "Despite having been used as a food colorant for many years, lycopene has received attention only recently with respect to its antioxidant activity and potential in preventing prostate cancer and cardiovascular diseases in humans. Such valuable have become these effects of lycopene on human health that they have led to the idea of increasing levels of lycopene in crops, particularly in tomatoes by genetic crosses in order to increase the lycopene content of the diets" (Bramley, 2000). "Natural mutants of tomatoes such as a high-pigment variety have been used in breeding strategies to alter lycopene levels" (Santos and Simon, 2002). Further,

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resorting to recombinant DNA technology, expression of bacterial and yeast genomes has been used to significantly alter lycopene levels in tomatoes (Fraser *et al.,* 2002; Mehta *et al.,* 2002). It is a matter of speculation whether increasing the content of lycopene in fruit will have a major influence on bioavailability as also the apprehensions to use GM tomato enriched in lycopene, like transgenic crops such as Bt brinjal (Tucker, 2003).

Chemistry, Isomerization and Degradation

Lycopene is a highly unsaturated, 40 carbon acyclic molecule containing 11 conjugated and 2 unconjugated double bonds arranged in all trans configuration in tomatoes; the most thermodynamically stable form. The acyclic structure of lycopene ensures its high solubility in organic solvents such as chloroform, benzene, hexane, acetone and petroleum ether. Chemical structure of lycopene is shown in Fig. 1.

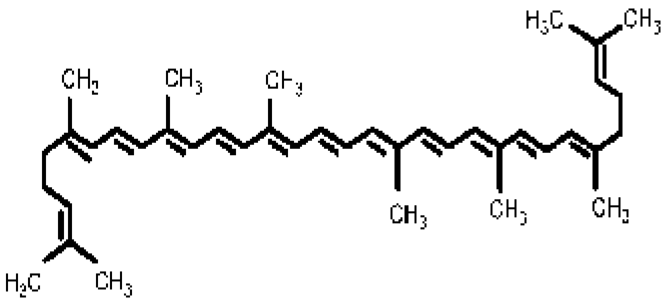

Fig.1. Chemical Structure of Lycopene

Physical Properties of Lycopene

Its chemicals formula - $C_{40}H_{56,}$ molecular mass - 536.85Da, melting point - 172-175^{0}C, color - dark reddish brown in powdered form, soluble in organic solvents and oil but not in water, ethanol and methanol and sensitive to light, oxygen, acids, high temperature, catalysts and inorganic metal ions.

The unique feature of lycopene structure is that "the seven double bonds can isomerize and form mono-or poly-cis isomers upon exposure to heat, light, and certain chemical reactions or during processing or storage. Interestingly, cis-isomers account for over 50% of the total lycopene in human serum and over 80% in tissues such as prostate". The cis-isomers are considered to be more polar and less prone to crystallization, but their formation in vivo and impact on host biology are poorly understood. Amongst the isomers of lycopene, 5- cis lycopene has been found to be 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) (Abushita *et al.,* 2000; Chasse *et al.,* 2001; Shi *et al.,* 2001; Allen *et al.,* 2002; Allen *et al.,* 2003; Hadley *et al.,* 2003; Campbell *et al.,* 2007).

Absorption and Distribution

Absorption of lycopene is similar to that of other lipid soluble compounds. It is absorbed across gastro intestinal tract via a chylomicron mediated mechanism, to be released into lymphatic system for transport to the liver. It gets stored in hepatocytes and to a lesser extent in spleen. In general 10-30 % of dietary lycopene is absorbed by humans, being equally absorbed from different sources of lycopene including tomato sauce, tomato juice or tomato oleoresin capsules. However, its absorption is influenced by several factors including the composition of food matrix, cooking temperature, presence of lipids, dosage and other soluble compounds including other carotenoids. These factors cause the release of lycopene from the food matrix enhancing its bioavailability (Re *et al.,* 2001; Unlu *et al.,* 2007).

Isomerization of lycopene affects its absorption efficiency as Cis-isomers are produced during processing and cooking of tomato products. In addition, some isomerization may occur in the gastrointestinal tract, especially in the environment of the stomach (Erdman, 2005). "It has been seen that when animals were fed lycopene containing all trans isomereric form, serum and tissue lycopene showed the presence of cis form. Cis-lycopene-rich tomato sauce has higher bioavailability than trans-rich tomato sauce in healthy adult subjects" (Micozzi *et al.,* 1992). Perhaps, all-trans-lycopene, a long linear molecule, may be less soluble in bile acid micelles. In contrast, cis-isomers of lycopene may move more efficiently across plasma membranes and preferentially incorporate into chylomicron (Johnson *et al.,* 1997). The interaction between the carotenoids in the ingested food influences the absorption of individual carotenoids (Rao and Agarwal, 2000; Bohm and Bitsch, 1999; Rao, 2000). Studies of humans consuming food with multiple carotenoids may increase or decrease the individual carotenoids in plasma, compared with those consuming purified carotenoids. However, such inferences and mechanisms yet remain to be streamlined. "It is well known that carotenoid–protein complexes are denatured by the cooking of vegetables and may impact bioavailability from the food matrix (Rao and Agarwal, 1998; Ryan *et al.,* 2008).

Lycopene being lipophilic and hydrophobic, its bioavailability is related to the presence of lipids in the diet. A study reported that salsa with the natural lipid source of avocado greatly enhanced carotenoid absorption from meals" (Unlu *et al.*, 2005). Similarly, the absorption of carotenoids from salad with low-fat salad dressing was impaired, compared with the absorption of carotenoids from salad with regular full-fat dressing. "It has been seen that ingestion of cooked tomato juice in oil medium increased serum lycopene levels by three folds where as consumption of an equivalent amount of unprocessed juice did not have any effect. Fielding *et al.,* 2005 showed that addition of olive oil to diced tomatoes during cooking greatly increases the absorption of lycopene.

Age may be another factor affecting lycopene absorption. The bioavailability of lycopene was less in those having age above 70 years compared to those having 20–35 years of age. However, there was no major difference in the bioavailability of β-carotene, α-carotene, and lutein (Cardinault *et al.,* 2003). Porrini *et al.,* 2005 suggested the eating behavior of different individuals makes the lycopene level vary among people.

The lycopene making its way into the blood from intestine is distributed throughout the body via circulatory system. It is the most predominant carotenoids in human blood plasma with a half life of about 2 to 3 days (Johnson *et al.,* 1997). The distribution of lycopene in human organs and plasma has been reported by Erdman (2005) where higher concentrations of lycopene were found in the liver, adrenal and reproductive tissues (ten times higher than other tissues), being within the concentration range of 0.2– 21.4 nmol/g tissue. Since lycopene is not deposited uniformly, the differences suggest that there are specific mechanisms for the preferential deposition of lycopene, particularly in the adrenals and testes. Studies have reported that lycopene concentration was highest in human testes, followed by adrenal gland > liver > prostate > breast > pancreas > skin > colon > ovary > lung > stomach >kidney > fat tissue > cervix" (Clinton *et al.,* 1996; Zaripheh *et al.,* 2003).

Lycopene as Antioxidant and Its Mechanism of Action

The reactivity of lycopene, or for that matter of human tissues carotenoids depends on their chemical structure, subcellular location and their capacity to interact with other antioxidants, concentration and the partial pressure of oxygen. Biochemically, lycopene seeks to become a scavenger of singlet oxygen ($^1O_2$) and peroxyl radical ($LOO^•$) oxidants. Lycopene lysis or can result in color loss on exposure to free radicals or oxidants. This is due to free radicals lycopene reaction causing interruption of the polyene chain, in which the conjugated double bond system may either be affected due to either cleavage or addition to one of the double bonds. The highly conjugated double bonds of lycopene play an all most important role in reactions involving energy transfer. Lycopene has quenching ability towards singlet oxygen ($^1O_2$), based on the excited energy which is greatly related to the length of the conjugated double bond system. Amongst all carotenoids, lycopene is the most efficient quencher of singlet oxygen with its quenching rate being two times higher than that of â-carotene and some ten times higher than that of á-tocopherol. Lycopene has been demonstrated to be the most potent antioxidant with the ranking: Lycopene > á- Tocopherol > á- carotene > â-Cryptoxanthin > Zeaxanthin = â-carotene > lutein. "Basically, chain lipid autoxidation reactions can be interrupted by antioxidants such as phenols, vitamin E and flavonoids, which eliminate the lipid peroxyl radicals by donating the hydrogen atom to form lipid peroxide and a resonance-stabilized antioxidant radical. However, as a carotenoid compound, lycopene may scavenge the radicals by more than one ways. (Krinsky and Johnson 2005; Gajic *et al.,* 2006).

Lycopene lies parallelly with the membrane surface. Though lycopene has limited interaction with aqueous phase radicals in the lipid bilayer as compared to more polar carotenoids such as zeaxanthin, yet it is still important in inhibiting lipid radicals at membranes as the first defense system of cells. Moreover, a combination of lycopene and other antioxidants is also important in scavenging of reactive species" (Johansson *et al.,* 1981; Lowe *et al.,* 1999 ; Young and Lowe, 2001).

Ionizing radiations may cause damage to living tissues by producing free radicals like reactive oxygen species (ROS) and reactive nitrogen species (RNS) which randomly react with lipids, proteins and nucleic acids of cells causing oxidative stress and damage to these macromolecules, leading to pathogenesis of chronic diseases and cancer. The first line of defense from the damaging effects of ROS is antioxidants, which convert the oxidants to less reactive species. This carotenoid lycopene has very strong antioxidant properties. The many studies confirm that dietary supplementation with LYC reduces risk of cancers of many organs, but also retard the growth of the tumors. Numerous *in vitro* and animal studies showed that LYC may provide protection against damages induced by ionizing radiation. It suggests that supplementation of LYC might be useful in diminishing of negative effect of cancer radiotherapy or in mitigating the effects of possible radiation accidents on human health (Gupta *et al.,* 2013, Kovacic and Osuna 2000; Gajowik *et al.,* 2014).

Of the carotenoids tested, lycopene has been demonstrated to be the most potent *in vitro* antioxidant leading many researchers to conclude that the antioxidant properties of lycopene are responsible for disease prevention (Erdman *et al.,* 2009). Analysis of the antioxidant status of blood in rats revealed that some antioxidant enzymes such as superoxide dismutase (SOD), glutathione reductase and glutathione peroxidase (GSHPx) can be induced by lycopene and GSH and phase II GST enzymes can also be increased. Dietary supplementation of lycopene resulted in significant increase in serum levels and decreased TBARS. Studies suggest that small amounts of tomato juice, tomato puree or other processed tomato products such as juices, soups or pasta sauces added to the diet over a short period can increase carotenoid concentration and provides protection from generalized DNA damage (Lauridsen *et al.,* 2000; Pool-Zobel *et al.,* 1997; Alshatwi *et al.,* 2010). Lycopene contains shielding methyl (-CH_3) groups and optimally positioned in LDL particles by its phytyl side chains to protect LDL against peroxidative modification along with maintaining its ability to act as ligand for LDL receptors. The other study reported that pretreatment of lycopene to ã-irradiated hepatocytes resulted in decreased lipid peroxidation and improved antioxidant status, thus preventing the cellular damage by inhibiting peroxidation of membrane lipids and free radicals induced DNA strand break formation. Likewise, the consumption of tomato products significantly enhanced the protection of lipoproteins to ex- vivo oxidative stress. In the same vein, another study demonstrated that incubation of plasma with lycopene protects LDL from copper induced oxidation reactions (Safari, 2007).

An eye disease, **Age related Macular Degeneration** (AMD) causes blindness in the aged people mostly of the developed world, the retina, especially the macula, is exposed to high levels of focused radiations in an equally high oxygenated environment. The concomitant presence of light and oxygen together provides for the generation of oxygen free radicals and singlet oxygen. Lycopene protects against such cataract development due to its antioxidant properties, and this can become useful for prophylaxis or therapy against cataracts. Lycopene supplementation in enucleated rat lenses culture has significantly restored **reduced glutathion**e along with antioxidant enzymes - **superoxide dismutase, catalase** and **glutathione S-transferase'** activities. similarly, one more study inferred that dietary tomatoes exercise a protective effect on both oxidative and nitrostative stress generated in the retinal pigment epithelium as become evident by reduced malondialdehyde level (Gupta *et al.,* 2003; Chichili *et al.,* 2006).

Interaction of Lycopene with other Antioxidants

"The combinations of lycopene and other antioxidants such as vitamin C, vitamin E and β-carotene have exhibited higher scavenging activity on 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical than that of their individual antioxidant activity. Besides, lycopene combined with other antioxidants also gave a better inhibiting effect towards diene hydroperoxides produced from linoleic methyl ester with 2,2'-azobis (2,4-dimethylvaleronitrile) (AMVN) induced oxidation. Lycopene has been also reported to help vitamin E and vitamin C in free radical quenching reactions" (Truscott, 1996).

As, lycopene has been reported to react effectively with vitamin E radical in the lipophilic compartment, its reaction with the hydrophilic vitamin C could be less effective. Lycopene is the strongest reducing agent and able to reduce the radical cations of lutein and zeaxanthin however β-carotene was not able to perform such an action" (Yeum *et al.,* 2004).

Preventive and Therapeutic Effects of Lycopene

Several studies have been reported that a diet rich in tomatoes and tomato products containing lycopene, protects against various chronic diseases by mitigating oxidative damage. Dietary lycopene protected lipids, proteins and DNA from oxidation. Such oxidized products have been thought to play an important role in cancer and chronic diseases and have been found to increase significantly in the chronic disease conditions. In addition, dietary intake of lycopene decreases the risk of chronic diseases with serum and tissue levels inversely related to the risk of these diseases. Several epidemiological studies have been published which show an inverse correlation with tomatoes and lycopene-rich diets and the incidence of several cancers and CHD. Though the beneficial effects are mainly attributed to its antioxidant properties yet other mechanisms like modulation of intercellular gap junction, communication, hormonal and immune system, metabolic pathways may also be involved (Fig. 2) (Wang *et al.,* 1996; Agarwal and Rao 2000).

Cancer

The evidence in support of lycopene in prevention of non communicable diseases (NCDs) comes from epidemiological studies as well as tissue culture studies using human cancer lines, animal studies and also human clinical trials (Jain *et al.,* 1999; Kotake-Nara *et al.,* 2001; Giovannucci *et al.,* 2002; Heath *et al.,* 2006; Rao 2006).

As for prevention of various types of cancers is concerned, lycopene stands out in the prevention of prostate cancer its role has been extensively studied with respect to prostate cancer. Evidently prostate cancer is the most common malignancy and cause of death in men. Though genetic factors and age are no less important determinants of the risk, environmental exposure, including diet, are increasingly being associated with the disease. A follow

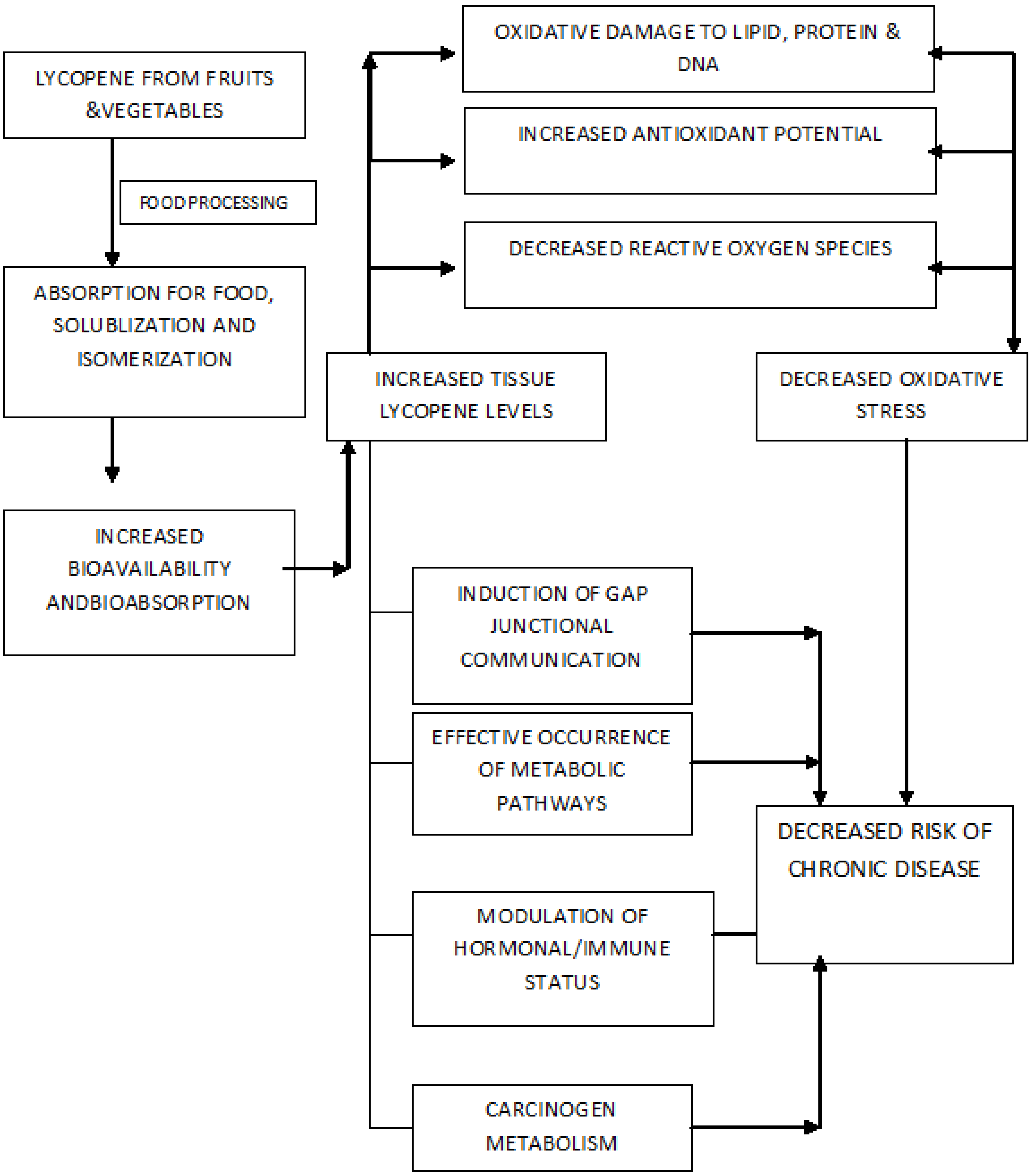

Fig. 2 Proposed Role of Lycopene in Human Health

up meta analysis of 72 different studies showed that lycopene intake as well as serum lycopene levels were inversely related to several cancers including prostate, breast, cervical, ovarian, liver and other organ sites. Several other studies since then demonstrated that with increased intake of lycopene and serum levels of lycopene, the risk of cancers were reduced significantly. Studies indicate that regular consumption of lycopene rich food has been reported to be associated with 30 to 40% lower risk of prostate cancer (Kucuk *et al.,* 2001; Bowen *et al.,* 2002; Giovannucci *et al.,* 2002).

Similarly, Heber and Lu (2002) reported that studies of human and animal cells have identified a gene, connexin 43, whose expression is up regulated by lycopene and that allows direct intercellular gap junctional communication (GJC). GJC is deficient in many human tumors and its restoration or upregulation is associated with decreased proliferation" (Heber and Lu, 2002; Kucuk *et al.,* 2002).

Lycopene rich tomato has been discussed as a potential effecter in the prevention and therapy of prostate cancer (Chen *et al.,* 2003). Overall epidemiological studies, *in vitro* tissue culture studies, animal studies and some human intervention studies are showing that increased intake of lycopene will result in increased circulatory and tissue levels of lycopene. *In vivo,* lycopene can act as a potent antioxidant and protect cells against oxidative damage and thereby prevent or reduce the risk of several cancers. Further studies are needed to get more proof and to gain better understanding of the mechanisms involved (Wang *et al.,* 1989; Levy *et al.,* 1995; Nagasawa *et al.,* 1995; Sharoni *et al.,* 1997).

Diabetes Mellitus

Lycopene is closely related to various metabolic complications, especially diabetes. Serum lycopene is inversely associated with type-2 diabetes and impaired glucose metabolism. The fact is proven by Coyne *et al.,* 2005 that plasma glucose and fasting insulin concentrations decreased significantly with increase in serum lycopene. Besides, Polidori *et al.,* 2000 found that plasma lycopene were significantly lower in very old diabetic patients as compared to controls, while significant inverse correlations were found between age and lycopene.

Cardiovascular Diseases

Cardiovascular disease (CVD) makes a dent on the normal function of the cardiovascular system involving heart and blood vessels. It is becoming one of the major causes of deaths in western world and an important contributor to morbidity and mortality in developing countries. The World Health Organization (WHO, 2009) reported that CVD is the world's largest killer which claims about 17 million lives a year. Tobacco use, unhealthy diet, physical inactivity and high intake of alcohol, increase the risk of CVD. Cumulative evidences in literature support the role of lycopene in the prevention of CVD. It has a protective effect against intimal wall thickness and myocardial infarction. The authors proposed that some other mechanism, besides its antioxidant effect, may be responsible for the protective effect. Similarly, another study concluded that low plasma lycopene concentration is associated with early atherosclerosis and increased intima media thickness of common carotid artery wall (CCA-IMT) (Rissanen *et al.,* 2002; WHO 2009)

Other Diseases

After ample evidence to recognize the role of lycopene as a potent antioxidant and its preventive role in oxidative stress mediated NCD's, scientists are beginning to explore investigate its role in other diseases afflicting human beings. Male infertility, a common reproductive disorder is now being associated with oxidative damage of the sperm leading to the loss of its quality and functionality. Significant levels of ROS are detectable in the semen of up to 25% of infertile men, where as fertile men do not produce detectable levels of ROS in their semen. Researchers are beginning to investigate the role of lycopene in protecting sperm from oxidative damage leading to infertility. Studies show that men with antibody mediated infertility were found to have lower serum lycopene levels than their fertile controls. In another study, a significant increase in serum lycopene concentration and improvement in sperm motility, sperm motility index, sperm morphology and functional sperm concentration was observed in infertile men when supplemented with 8 mg lycopene for 12 months. Furthermore, it was found lycopene treatment resulted in 36% successful pregnancies (Zini *et al.,* 1993; Palan and Naz 1996)

Oxidative stress may contribute to the pathogenesis of skeletal system including osteoporosis, the most prevalent 'metabolic bone disease' Lycopene has a stimulatory effect on cell proliferation and the differentiation marker alkaline phosphatase of osteoblasts, as also an inhibitory effects on osteoclasts formation and resorption.There have been results of a possible decrease in bone turnover and oxidative stress markers and an increase in antioxidant status in postmenopausal women taking tomato juice or lycopene capsules. Thus lycopene plays a role in bone health and provides dietary alternative to drug therapy for women who are at risk of osteoporosis (Ishimi *et al.,* 1999; Kim *et al.,* 2003)

High blood pressure, a 'silent killer,' is a disorder in which symptoms are not observed until a more advanced and a fatal stage is reached. The antioxidant property of lycopene has attracted scientific research into its protective role in hypertension. A recent study showed that lycopene supplementation at 15 mg/ day for 8 weeks, significantly decreased systolic blood pressures from 144mm Hg to 134 mm Hg in mildly hypertensive subjects. In another study a significant reduction in plasma lycopene was observed in the hypertensive patients compared to normal subjects. Recognizing the importance of antioxidants in the management of hypertension, a dietary approach to control hypertension (DASH) is recommended that contains substantially higher levels of lycopene along with other carotenoids, polyphenols, flavanols, flavanones and flavan-3-ols (Paran and Engelhard, 2001; Moriel *et al.,* 2002; Most, 2004; Paran, 2006).

Brain is a vulnerable organ for oxidative damage due to high levels of oxygen uptake and utilization, high lipid content and low antioxidant capacity. Rao and Balachandran (2003) suggested the role of lycopene in neurodegenerative diseases including Alzeheimers disease. Lycopene was shown to cross the blood brain barrier and be present in central nervous system (CNS) in low concentration. Significant reduction in the levels of lycopene was reported in patients suffering from Parkinson's disease and vascular dementia. Likewise, tomato ingestion might serve as a preventive therapy against neurodegenerative diseases such as Parkinson's disease caused by 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) and other environmental toxins. Moreover, it was also suggested to provide protection against amyotrophic lateral sclerosis (ALS) disorder in humans (Foy *et al.,* 1999; Longnecker *et al.,* 2000; Suganuma *et al.,* 2002; Rao and Balachandran, 2003).

Intake of tomatoes was also inversely and significantly associated with respiratory infections. A study showed protective role of lycopene in the prevention of emphysema in a mouse model. At a conference held to deliberate on the role of processed tomatoes in human health, data was provided for the protective role of lycopene in the prevention of emphysema in Japanese population.Lycopene plays an important role in the protection against photoxidative processes by acting as singlet molecular oxygen and peroxyl radicals scavengers. Further it can interact synergistically with other antioxidants. Ingestion of tomato paste daily for 10 weeks, protected against UV light induced erythema on the dorsal skin. However, lycopene is completely depleted from skin upon exposure to solar radiation and undergoes oxidative or enzymatic cleavage to form apocarotenoids (Tang *et al.,* 1991; Ribaya *et al.,* 1995; Stahl *et al.,* 2001; Rao and Rao 2007).

It has been reported that persons with a high intake of carotene, there is reduction in the incidence of risk of cataract and the relationship between nuclear cataract and intakes of α-carotene, β -carotene, lutein, lycopene and cryptoxanthin stratifyied by gender and regular multivitamin use It has been reported that lycopene prevents cataractogenesis in vivo and *in vitro* by virtue of its antioxidant properties. In previous studies, it was found that lycopene prevented sugar-induced diabetic cataract. Several findings indicate that lycopene is an important part of the human organism's natural defense mechanism that protects us from harmful oxidizing agents. Lower serum lycopene levels were also reported in human immuno deficiency virus (HIV) positive women and children (Cumming *et al.,* 2000; Mohanty *et al.,* 2002)

The scientific interest in devising innovative strategies to affect the prevention of human diseases reveals the common etiological and etiogenesis of these diseases. Oxidation of cellular components as an initial cause eventually leading to the incidence of several disease brings the focus to the usage of antioxidants as cure. Lycopene, being a potent antioxidant can prevent the genesis and progression of many human diseases nipping the evil in the bud and improving the quality and period of life.

Lycopene-rich by-products from Food Processing

Food processing by-products from the tomato puree and sauce industry are commonly used in the development of lycopene-rich products. Previously, Al-Wandawi *et al.,*1985 had reported that tomato skins contained a high amount of lycopene. Food processing waste is commonly used as feed for livestock. Among the agro-industrial by-products (cereal and pulsed, distillery, oil-seeds, sugar industry, textile industry, vegetables and fruits industry, vegetables crop, and miscellancous), tomato wastes are the only by-products that are rich in lycopene.

Nowadays, there is an increasing trend towards utilization of food processing by-products as a source of functional components (Schieber *et al.,* 2001). Many studies have been carried out on the extraction of lycopene from by-products, especially tomato waste. Optimization of the solvent extraction procedure was also performed to obtain a maximum lycopene yield from tomato peels using response surface methodology (Kaur *et al.,* 2008). Application of high hydrostatic pressure processing without heating was reported to provide an increased yield of lycopene from tomato paste waste (Jun, 2006). High pressure processing of tomato paste waste for 1 min gives a higher lycopene yield than solvent extraction for 30 min (Xi, 2006). The Extractor Naviglio has been introduced to obtain higher purity lycopene from tomato by-products through pressurized extraction (Naviglio *et al.,* 2008a; 2008b). This extraction method requires tap water as extracting solvent with minimum organic solvent and the by-products can be further used as livestock feed. Furthermore, enzymatic treatment using cellulase and pectinase could offer one fold higher yield in the recovery of lycopene from tomato waste (Choudhari and Ananthnarayanan, 2007). Lavecchia and Zuorro, 2008 also reported that enzymatic treatment on tomato peels was able to increase the lycopene yield 20-fold. Moreover, supercritical fluid extraction has been applied in extraction of lycopene from several by-products" (Rozzi *et al.*, 2002; Nobre *et al.,* 2006; Vagi *et al.,* 2007).

Optimization of different extraction parameters on lycopene-rich by-products using supercritical fluid extraction have also been studied by researchers (Sandei and Leoni, 2006; Topal *et al.,* 2006; Kassama *et al.,* 2008). "Supercritical fluid extract of lycopene-rich tomato pulp waste has been used for encapsulation using an emulsion system in combination with gelatin and poly γ-glutamic acid (γ-PGA) as coating materials" (Chiu *et al.,* 2007).

There have been initiatives by food scientists to recycle the lycopene-rich by-products as food ingredients. Fortification with lycopene in dry fermented sausage was also done by adding dried tomato peel to the meat mixture during the sausage production (Calvo *et al.,* 2008). "The development of extrusion processing using barley-tomato pomace blends and processing into snacks has been demonstrated by Altan *et al.,* 2008**.** Besides, enrichment of low quality edible oils such as refined olive oil, extra virgin olive oil and refined sunflower oil by lycopene from tomato peels or tomato puree was proven to induce thermal stability to these edible oils (Benakmoum *et al.,* 2008). The idea of using lycopene-rich by-products from tomato peel and seed for hen feed will further enrich the egg yolk with lycopene. However, only low amounts of lycopene were found to be transferred to the egg yolk (0.1% from tomato peels and 0.7% from tomato seeds) (Knoblich *et al.,* 2005). Another study also determined the quality of lycopene-rich by-products after food processing such as blanching and drying, where blanching in hot water at 75 °C for 2 min could help to reduce the drying time and increase the lycopene bio-availability (Dhas *et al.,* 2004).

Estimation of Dietary Intake Levels

Populations the world over, are estimated to consume less than 2mg of lycopene per day. It is evident that the average intake levels of lycopene are much lower than required to provide its beneficial effects. Although the beneficial effects of lycopene in the prevention of human diseases have been well documented it is not yet recognized as an essential nutrient. As a result there is no official recommended nutrient intake (RNI) level set by health professionals and government regulatory agencies. However based on reported studies, a daily intake level of 5-7mg in normal healthy human beings may be sufficient to maintain circulating levels of lycopene at levels sufficient to combat oxidative stress and prevent chronic diseases. Under the condition of disease such as cancer and cardiovascular, much higher levels of lycopene ranging from 3 to 4 times of the required levels per day may be required (Rao 2002; Rao and Shen, 2002;Heath *et al.,* 2006).

Safety Evaluation

The safety aspect of bioactive compounds in products has been received much attention from food scientists to avoid any side effects. Either synthetic lycopene or that from natural sources have been reported to be safe (Generally Recognized as Safe, GRAS grade) when used as food additive. Several studies have been conducted to evaluate acute toxicity, sub chronic and chronic safety as well as reproductive effects and genotoxicity. Long back, a single dose of 3g/kg crystalline (unformulated) lycopene was administered by various routes. There were no adverse effects with orally or intraperitoneally administered lycopene. However, a transient decrease in body tone was observed when lycopene was given subcutaneously. Furthermore, up to 3g/kg/day of formulated lycopene exhibited no effects on body weight, hematology, blood chemistry, ophthalmologic variables or histology in rats.

Consumption of 1g/kg/day of formulated lycopene during gestation resulted in no signs of maternal toxicity or teratogenic effects in rats. Furthermore, there was no mutagenic activity for formulated lycopene. However, the degradation products of crystalline lycopene formed by the exposure to light and air were shown to exhibit some mutagenic activity. A study reported that high intake of lycopene containing food, (~2L of tomato juice daily for several years) resulted in orange discolouration of skin lycopenemia. Although there were deposits of lycopene and fatty deposits in the liver but there was no hepatic dysfunction. Moreover, the discoloration faded after 3 weeks by consuming a diet free of tomato juice. Thus, there are no adverse effects and it is safe to consume dietary or formulated lycopene (McClain and Bausch, 2003).

Thus with its broad spectrum of potential applications to human health, lycopene is being considered as a functional ingredient having neutraceutical properties. The emerging area of complementary healthcare offers many opportunities for food products containing compounds such as lycopene. Itwould be of great interest to the food related industries as well as to public health organizations. However, the aspect calls for prudent and purposeful investigations.

Conclusion

Lycopene, the red pigment that was used as a food colorant for a longtime, has also been found to be a powerful antioxidant with strong prospects to prevent non-communicable diseases. Beneficial role of lycopene consumption synergizes on its interaction with other bioactive substances of phytochemical origin to play optimum role in human health enhancement. Since genesis and development of NCD's involve oxidative stress, several clinical trials have indicated the role of lycopene in attenuating oxidative stress, the major reason for the occurrence of these diseases. More knowledge of lycopene, absorption, bioavailability, metabolism, mode of action, safe intake levels and its interaction with other phytochemicals will go a long way in harnessing lycopene usage to quell oxidative stress and to make it act as it means of intervention against NCD's.

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