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Tomato Lycopene –A review

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Abstract:

Lycopene is a bright red carotene and carotenoid pigment and phytochemical found in tomatoes and other red fruits and vegetables, such as red carrots, red bell peppers, watermelons, and papayas (but not strawberries or cherries). Although lycopene is chemically a carotene, it has no vitamin A activity. Foods that are not red may contain lycopene as well. The antioxidant properties of lycopene are thought to be primarily responsible for its beneficial properties .Data concerning lycopene bioavailability, tissue distribution, metabolism, excretion, and biological actions in experimental animals and humans are beginning to accumulate although much additional research is necessary. Although promising data from epidemiological, as well as cell culture and animal, studies suggest that lycopene and the consumption of lycopene containing foods may affect cancer or cardiovascular disease risk, more clinical trial data is needed to support this hypothesis. In addition, future studies are required to understand the mechanism(s) whereby lycopene or its metabolites are proven to possess biological activity in humans.

Keywords: *Lycopene, Carotenoids, Oxidative stress ,Antioxidant, ChronicDiseases*

I. Introduction:

In plants, algae, and other photosynthetic organisms, lycopene is an important intermediate in the biosynthesis of many carotenoids, including beta carotene, responsible for yellow, orange or red pigmentation, photosynthesis, and photo-protection. Like all carotenoids, lycopene is a polyunsaturated hydrocarbon (an unsubstituted alkene). Structurally, it is a tetraterpene assembled from eight isoprene units, composed entirely of carbon and hydrogen, and is insoluble in water. Lycopene's eleven conjugated double bonds give it its deep red color and are responsible for its antioxidant activity. Due to its strong color and non-toxicity, lycopene is a useful food coloring and is approved for usage in some countries.

Lycopene is more bioavailable from tomato paste than from fresh tomatoes:

Lycopene bioavailability from a single dose of fresh tomatoes or tomato paste (23 mg lycopene) ingested together with 15 g corn oil was compared by analyzing carotenoid concentrations in the chylomicron

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fraction. The lycopene isomer pattern was the same in both fresh tomatoes and tomato paste. The triacylglycerol response in chylomicrons was not significantly different after both treatments. Ingestion of tomato paste was found to yield 2.5-fold higher total and all-trans-lycopene peak concentrations ($P < 0.05$ and $P < 0.005$, respectively) and 3.8-fold higher area under the curve (AUC) responses ($P < 0.001$) than ingestion of fresh tomatoes. The same was calculated for lycopene cis-isomers, but only the AUC response for the cis-isomers was significantly higher after ingestion of tomato paste ($P < 0.005$). No difference was observed in the alpha- and beta-carotene response. Thus, in humans, the bioavailability of lycopene is greater from tomato paste than from fresh tomatoes.[1]

Lycopene, Tomato Products, and Prostate Cancer Incidence:

Lycopene has been proposed to protect against prostate cancer through various properties including decreased lipid oxidation, inhibition of cancer cell proliferation, and most notably potent antioxidant properties. Epidemiologic studies on the association between lycopene and prostate cancer incidence have yielded mixed results. Lycopene content of tomatoes andTomatoes are an integral part of diet world wide. Many population studies have established link between dietary intake of tomatoes, a major source of a carotenoid antioxidant lycopene and reduced risk of chronic diseases. This study evaluates the lycopene contents of various commonly consumed tomato products and estimates its daily intake levels. A fast and simple spectrophotometric method for routine analysis of lycopene was developed and validated against HPLC method. Lycopene content in various tomato products ranged from 42 ppm to 365 ppm. Average daily dietary lycopene intake levels were assessed by administering food frequency questionnaire and were estimated to be 25.2 mg day−1. Fresh tomatoes accounted for 50% of total lycopene intake. Tomato products and their contribution to dietary lycopene.[2]

Lycopene Sources:

Some of the fruits and vegetables rich in lycopene include pink grapefruit, papaya, wolfberry, goji, and tomatoes. For the vast majority of people, the most common dietary sources of lycopene remains, tomatoes, tomato-based sauces, juices, and ketchup.

It should be noted that eating raw tomatoes provides only a small amount of bioavailable lycopene. This is because the lycopene in raw tomatoes is tightly bound to indigestible fiber that prevents much of the nutrients from being absorbed by your body. On the other hand, cooked tomato products such as tomato paste or tomato sauce, are a much better source of dietary lycopene. As far as the health of your skin is concerned, even eating cooked tomatoes may not deliver sufficient lycopene to your skin. After ingestion, lycopene is eventually released into your lymphatic system and distributed throughout your whole body. Unfortunately, it is mostly deposited in fat-rich organs like your adrenal glands, colon, and liver. In the end, only a small fraction of the lycopene you eat ever reaches your skin.

However, the fat soluble nature and relatively small molecule size of this powerful plant nutrient make it easily absorbed when applied topically in a cream or lotion. Moreover, because lycopene is especially effective in tissues with high fat content, the lipid-rich environment of the skin provides a very receptive target for its potent anti-aging benefits.[3]

The Many Anti-Aging Benefits of Lycopene:

Lycopene's powerful antioxidant action and ability to defend your skin against UV radiation are due in large part to its unique molecular design, which is responsible for lycopene's red appearance and its ability to block UV light. Though lycopene's sun protection is only equivalent to approximately SPF-3 and isn't adequate sun protection by itself, it is still a valuable added benefit for your skin.In fact, a study conducted by the Department of Dermatology at the Mount Sinai School of Medicine, examined topically-applied lycopene's ability to defend against the harmful effects of UVB radiation. It was found that topical application of lycopene suppressed the typical UVB-induced activity of an enzyme called ornithine decarboxylase, an important initiating and rate-controlling factor involved in stabilizing DNA structure in the nucleus of the skin cells as well as maintaining the DNA double strand-break repair pathway. What this means is that lycopene was able to offer significant protection to the cellular DNA and thus negated the need for the body to activate its internal DNA repair pathways.

The same study also revealed that UVB radiation depleted an important substance in your skin known as PCNA (proliferating cell nuclear antigen), which is vital for DNA synthesis and cell repair. The topical application of lycopene was found to reverse the reduction of PCNA caused by UVB exposure to a significant degree. In addition, it was shown that lycopene may also protect your skin through its ability to reduce inflammation, encourage cell renewal, and inhibit normal DNA damage following UVB injury.[4]

Epidemiological evidence

Risk of cancer:

The Mediterranean diet, which is rich in vegetables and fruits, including tomatoes, has been suggested to be responsiblefor the lower cancer rates in that region. Dietary intake of tomatoes and tomato products has been found tobe associated with a lower risk of a variety of cancers in severalepidemiologicalstudies.A high intake of tomatoes was linked to protective effects against digestive tract cancers in a case–control study and a 50% reduction in rates of death from cancers at all sites in an elderly US population. The most impressive results come from the US Health Professionals Follow-up Study, which evaluated the intake of various carotenoids and retinol, from a food-frequency questionnaire, in relation to risk of prostate cancer. The estimated intake of lycopene from various tomato products was inversely related to the risk of prostate cancer. This result was not observed with any other carotenoid. A reduction in risk of almost 35% was observed for a consumption frequency of 10 or more servings of tomato products per week, and the protective effects were even stronger with more advanced or aggressive prostate cancer. In recent studies serum and tissue levels of lycopene were shown to be inversely associated with the risk of breast cancer and prostate cancer; no significant association with other important carotenoids, including β-carotene, was observed.[5]

Risk of cardiovascular disease:

Oxidation of low-density lipoproteins, which carry cholesterol into the blood stream, may play an important role in the causation of atherosclerosis. Antioxidant nutrients are believed to slow the progression of

atherosclerosis because of their ability to inhibit damaging oxidative processes. Several controlled clinical trials and epidemiological studies have provided evidence for the protective effect of vitamin E, which has been ascribed to its antioxidant properties. However, in the recently completed Heart Outcomes Prevention (HOPE) Study, supplementation with 400 IU/d of vitamin E for 4.5 years did not result in any beneficial effects on cardiovascular events in patients at high risk. In contrast, other studies indicated that consuming tomatoes and tomato products containing lycopene reduced the risk of cardiovascular disease.[6][7]

Lycopene isomerisation:

The seven double bonds can isomerize and form mono- or poly-cis isomers upon exposure to heat, light, 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 how they form in vivo and their impact on host biology is 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 transisomer).Lycopene degradation occurs with light, heat, oxygen,

metallic ions of copper and iron catalyzing oxidation andacids.The potential of these non-enzymatic reactions toaffect lycopene destruction in vivo is uncertain, but is critical when considering laboratory investigations of carotenoids in cell culture and in animal models.Carotenoids are not inherently stable in vitro and degradation occurs quickly under standard conditions of cell culture Rodent studies also require careful consideration regarding lycopene stability. Lycopene,either as a pure agent or as part of tomato components,can be incorporated into semi-purified diets for studies of carcinogenesis or tumorigenesis. Again, careful documentation of concentrations of carotenoids in the ingredients, the formulated diet, and stability under conditions of feeding are essential components of sound scientific technique. Ambient lighting during formulation and the potential of heating and drying processes during pelleting contribute to significant degradation, therefore,is a key consideration.[8][9]

Tomato lycopene and its role in human health and chronic diseases:

Epidemiological evidence

Risk of cancer:

The Mediterranean diet, which is rich in vegetables and fruits, including tomatoes, has been suggested to be responsible for the lower cancer rates in that region.[10]. Dietary intake of tomatoes and tomato products has been found to be associated with a lower risk of a variety of cancers in several epidemiological studies. A high intake of tomatoes was linked to protective effects against digestive tract cancers in a case-control study and a 50% reduction in rates of death from cancers at all sites in an elderly US population.[11] The most impressive results come from the US Health Professionals Follow-up Study, which evaluated the intake of various carotenoids and retinol, from a food-frequency questionnaire, in relation to risk of prostate cancer.[12] The estimated intake of lycopene from various tomato products was inversely related to the risk of prostate

cancer. This result was not observed with any other carotenoid. A reduction in risk of almost 35% was observed for a consumption frequency of 10 or more servings of tomato products per week, and the protective effects were even stronger with more advanced or aggressive prostate cancer. In recent studies serum and tissue levels of lycopene were shown to be inversely associated with the risk of breast cancer and prostate cancer; no significant association with other important carotenoids, including β-carotene, was observed. Giovannucci50 recently reviewed 72 epidemiological studies, including ecological, case-control, dietary and blood-specimen-based investigations of tomatoes, tomato-based products, lycopene and cancer. In 57 studies there was an inverse association between tomato intake or circulating lycopene levels and risk of several types of cancer; in 35 cases the association was statistically significant. None of the studies showed adverse effects of high tomato intake or high lycopene levels.

Although the epidemiological evidence of the role of lycopene in cancer prevention is persuasive, this role remains to be proven. There are few human intervention trials investigating the effectiveness of lycopene in lowering cancer risk. Most of the workers have investigated the effects of tomato or tomato product (lycopene) supplementation on oxidative damage to lipids, proteins and DNA[13].A preliminary report has indicated that tomato extract supplementation in the form of oleoresin capsules lowers the levels of prostate-specific antigen in patients with prostate cancer.[14]

Risk of cardiovascular disease:

Oxidation of low-density lipoproteins, which carry cholesterol into the blood stream, may play an important role in the causation of atherosclerosis.[15] Antioxidant nutrients are believed to slow the progression of atherosclerosis because of their ability to inhibit damaging oxidative processes. Several controlled clinical trials and epidemiological studies have provided evidence for the protective effect of vitamin E, which has been ascribed to its antioxidant properties. However, in the recently completed Heart Outcomes Prevention Evaluation (HOPE) Study, supplementation with 400 IU/d of vitamin E for 4.5 years did not result in any beneficial effects on cardiovascular events in patients at high risk.63 In contrast, other studies indicated that consuming tomatoes and tomato products containing lycopene reduced the risk of cardiovascular disease.[16]

In a multicentre case-control study, the relation between antioxidant status and acute myocardial infarction was evaluated. Subjects were recruited from 10 European countries to maximize the variability in exposure within the study. Adipose tissue antioxidant levels, which are better indicators of long-term exposure than blood antioxidant levels, were used as markers of antioxidant status. Biopsy specimens of adipose tissue were taken directly after the infarction and were analysed for various carotenoids. After adjustment for a range of dietary variables, only lycopene levels, and not β-carotene levels, were found to be protective.

A study from Johns Hopkins University, Baltimore, showed that smokers with low levels of circulating carotenoids were at increased risk for subsequent myocardial infarction[17].Lower blood lycopene levels were

also found to be associated with increased risk for and death from coronary artery disease in a population study comparing Lithuanian and Swedish cohorts with different rates of death from coronary artery disease.

Role of Lycopene in Other Diseases: Researchers have started to investigate role of lycopene in various human diseases, because of its recognition as a potent antioxidant and its preventive role in oxidative stress mediated chronic diseases.

Osteoporosis: Oxidative stress may be one of the contributing factors involved in the pathogenesis of skeletal system like development of osteoporosis, which is the most common metabolic bone disease. Lycopene has a stimulatory effect on cell proliferation and the differentiation marker alkaline phosphatase of osteoblasts as well as 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 key role in maintaining bone health and provides dietary alternative to drug therapy especially for women with the risk of this disease [18][19]

Male Infertility: It is the most common male reproductive disorder is now being associated with oxidative damage of the sperm which leads to the loss of its quality and functionality. Significant levels of ROS are detectable in the semen of up to 25 % of infertile men whereas fertile men do not produce detectable levels of ROS in their semen[20]. 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 [21]. According to other study, a significant increase in serum lycopene concentration and improvement in sperm motility, sperm motility index, sperm morphology and functional sperm concentration was reported in infertile men when administered with 8 mg lycopene for 12 months. Furthermore, it was found lycopene treatment resulted in 36 % successful pregnancies.

Hypertension: Hypertension, a ‘silent killer,' is a disorder which is asymptomatic until a more advanced and a fatal stage is reached. Lycopene’s antioxidant property has attracted scientific research into its protective role in hypertension. As per recent study it was demonstrated that lycopene supplementation of 15 mg/ day for 8 weeks remarkably decreased systolic blood pressures from baseline values to 144 mm 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. As the antioxidants are important in the management of hypertension, a ‘dietary approach for controlling hypertension (DASH)', diet containing substantially higher levels of lycopene along with other carotenoids, polyphenols, flavanols, flavanones and flavan-3-ols is recommended.[22]

Neurodegenerative Diseases: It was reported that lycopene was able 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 74. Similarly, Suganuma et al., 75 reported that 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 [23].

Respiratory Infections: Intake of tomatoes was also inversely and significantly associated with respiratory infections. A study demonstrated that lycopene has a protective role for 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 lycopene's protective role for emphysema's prevention in Japanese population [24]

Cataract: It was reported that persons with a high intake of carotene showed reduced incidence of risk of cataract and the relationship between nuclear cataract and intakes of α- carotene, β- carotene, lutein, lycopene and cryptoxanthin stratifying by gender and by regular multivitamin use . It has been confirmed that lycopene prevents cataract genesis in-vivo and in-vitro due to its antioxidant potentials . In previous studies, it was found that lycopene prevented sugar induced diabetic cataract [25].

Erythema: Lycopene plays an important role in the protection against photoxidative processes. It acts as singlet molecular oxygen and peroxylradicals scavengers. It can also interact synergistically with other antioxidants. Administration of tomato paste daily for 10 weeks, protected against UV light induced erythema on the dorsal skin. However, it is completely depleted from skin upon exposure to solar radiation and undergoes oxidative or enzymatic cleavage to form apocarotenoids [26]

Diarrhoea: In a prospective study, Fawazi et al., found that an intake of tomatoes for 2-3 days compared with zero days has been associated with significant reduction in mortality (48%) and with a decreased risk of death associated with diarrhoea.

HIV: Several studies indicate that lycopene plays important role in the human organism's natural defense mechanism which gives protection from the harmful oxidizing agents. Lower serum lycopene levels were also reported in human immuno deficiency virus (HIV) positive women and children. Further investigations can explore lycopene's role in various human diseases like diabetes, rheumatoid arthritis, periodontal diseases and inflammatory disorders 38. Antioxidant potential of lycopene are opening up new applications in pharmaceutical; nutraceutical and cosmeceutical products and can inhibit the progression or development of many human diseases at an initial stage and may improve the quality of life [27].

II. Conclusion:

The effect of lycopene on tumor cell shows that lycopene restricts different cancer cells, e.g., prostate cancer cells. Moreover, different methods are available for lycopene extraction, but the supercritical fluid extraction of Lycopene with CO_2 gives better results than other methods. The extracted lycopene can be inserted into the diet, where natural sources of lycopene are not available. In some industrial processes, where oxygen quenching is required, extracted lycopene can be used. The experiments showed that heat-processed food gives a larger amount of available Lycopene than that was previous, but the degradation of extracted lycopene is greater at high-temperature environments. These controversial characteristics are still unexplained. For human dietary, Purposes lycopene should be one of the critical compounds because of its nutraceutical, epidemiological, and pharmaceutical importance.

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