REVIEW

LYCOPENE – ROLE IN HEALTH AND DISEASE

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ABSTRACT

Tomatoes are rich in lycopene, a hydrocarbon antioxidant that is the source of the red coloring in ripe tomatoes. The potential benefits of nutritional antioxidants such as lycopene have received a great deal of attention in the present days. As tomatoes are an important constituent of our diet and are relatively cheaper than various commercial preparations available in market, more and more interest is arising regarding their therapeutic benefits in various diseases. This review highlights the importance of Lycopene in maintaining normal health and its role in various diseases.

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INTRODUCTION

Carotenoids are a class of more than 600 naturally occurring pigments synthesized by plants, algae, and photosynthetic bacteria. These richly coloured molecules are the sources of yellow, orange, and red colours of many plants. Fruits and vegetables provide most of the Carotenoids in the human diet. Alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein, lycopene, and zeaxanthin are the most common dietary carotenoids. Alpha-carotene, beta-carotene and beta-cryptoxanthin are provitamin A carotenoids, meaning they can be converted by the body to retinol. Lutein, lycopene, and zeaxanthin cannot be converted to retinol, so they have no vitamin A activity. Carotenoids can be broadly classified into two classes, carotenes (alpha-carotene, beta-carotene, and lycopene) and xanthophylls (beta-cryptoxanthin, lutein, and zeaxanthin).

Oxidative stress, induced by Reactive oxygen species (ROS), is associated with the incidence of chronic diseases such as cancer, coronary heart disease (CHD) and osteoporosis . ROS are highly reactive oxidant molecules that are generated endogenously through normal metabolic processes, life style activity and the diet. Antioxidants provide an effective means to combat the deleterious effects of ROS and are increasingly being considered as strategic chemopreventive agents in the management of human diseases.

Lycopene, a carotenoid phytonutrient, is the most potent antioxidant naturally present in many fruits and vegetables. However, tomatoes and processed tomato products constitute the major source of dietary lycopene accounting for up to 85% of the daily intake

CHEMISTRY, BIOAVAILABILITY AND METABOLISM OF LYCOPENE

Lycopene is a highly unsaturated straight chain hydrocarbon with a total of 13 double bonds, 11 of which are conjugated. This unique nature of the lycopene molecule makes it a very potent antioxidant. Although in nature it exists predominantly in its all-trans isomeric form, it can undergo light, thermal energy and chemical reaction induced cis-isomerization. Lycopene absorption has been shown to be significantly higher in the thermally

processed tomato products compared to raw tomatoes, and the processed products were shown to contain higher levels of cis-isomers of lycopene. It is therefore thought that cis-isomerization of lycopene enhance its absorption. For dietary carotenoids to be absorbed intestinally, they must be released from the food matrix and incorporated into mixed micelles (mixtures of bile salts and several types of lipids). Therefore, carotenoid absorption requires the presence of fat in a meal. As little as 3-5 g of fat in a meal appears sufficient to ensure carotenoid absorption. Because they do not need to be released from the plant matrix, carotenoids supplements are more efficiently absorbed than carotenoids in food. Within the cells that line the intestine (enterocytes), carotenoids are incorporated into triglyceride-rich lipoproteins called chylomicrons and released into the circulation. Triglycerides are depleted from circulating chylomicrons through the activity of an enzyme called lipoprotein lipase, resulting in the formation of chylomicron remnants. Chylomicron remnants are taken up by the liver, where carotenoids are incorporated into lipoproteins and secreted back into the circulation. In the intestine and the liver, provitamin A carotenoids may be cleaved to produce retinal, a form of vitamin A. The conversion of provitamin A carotenoids to vitamin A is influenced by the vitamin A status of the individual. Although the regulatory mechanism is not yet clear in humans, cleavage of provitamin A carotenoids appears to be inhibited when vitamin A stores are high.

SOURCES

Tomatoes, pink grapefruit, watermelon, and guava. In tomatoes, lycopene content is affected by the specific variety of tomato and by ripening stage. Deep red varieties contain up to 50 mg/kg, while yellow tomatoes may be as low as 5 mg/kg. Bioavailability of lycopene is improved with cooking.

Lycopene Content of Selected Foods

Food	Serving	Lycopene
Tomato Paste, Canned	1 cup	75,362
Tomato Puree, Canned	1 cup	54,385
Tomato Soup, Canned	1 cup	25,615
Tomato Juice, Canned	1 cup	21,960
Watermelon, Raw	1 wedge	12,962
Tomatoes, Raw	1 cup	4,631
Ketchup	1 tablespoon	2,551

BIOLOGICAL ACTIVITY

Carotenoids are protective against chronic diseases which are thought to be caused by damage from free radicals. Free radicals are molecules with an unpaired electron in their outer atomic orbital, causing the molecule to be extremely reactive. Carotenoids prevent oxidative damage in biological systems, such as damage to the cell membrane and other structures, DNA molecules, lipids, and proteins.

MECHANISM OF ACTION

- antioxidant activity
- inhibition of cancer cell proliferation
- interference with growth factors stimulation of cancer cell proliferation
- cancer prevention by inducing phase ii enzymes
- regulation of transcription
- restoration of gap junctions.

ROLE IN ORAL AND GENERAL HEALTH

LEUKOPLAKIA

Tobacco smoke contains NOO_ radicals, which are carcinogenic. Free radical scavengers should be the necessary part of the treatment regimen in tobacco chewers or smokers to prevent the formation, induce the remission or inhibit the progression of pre-cancerous lesions into malignancies. Lycopene exhibits the highest physical quenching rate constant with singlet oxygen. Lycopene increases the expression of a gene encoding connexin-43, a gap junction protein, effect being independent of pro vitamin-A or antioxidant properties.

LICHEN PLANUS

NAGAO T etal reported significantly lower levels of serum lycopene in the patients with atrophic and erosive lichen planus as compared to healthy controls. Role of lower levels of this antioxidant in the pathogenesis of this disease process can not be ruled out & lycopene supplementation may be used in treatment. Though the exact role of free radicals in the pathogenesis of OLP is not established, many studies have suggested oxidative stress to play vital role .Lycopene being a potent antioxidant may have an important role to play in prevention.

OSMF

Though the exact role of Lycopene in treating OSMF is still controversial, certain studies have revealed the benefitial effect of this Carotenoid in increasing the mouth opening in OSMF.

CANCER

Oxidative stress is recogonized as one of the main contributors to increased risk of Cancer and Lycopene being a potent antioxidant has been found to inhibit proliferation of several types of human cancer cells.

PROSTATE CANCER

There is a strong link between

lycopene and prostate cancer. Using the cumulative average of the three dietary questionnaires used in the Health

Professionals Follow-Up Study (HPFS), it was determined that lycopene intake was associated with reduced risk of prostate cancer. Intake of tomato sauce, the primary source of bioavailable lycopene, was associated with an even greater reduction in prostate cancer.

BLADDER, CERVICAL, BREAST, AND LUNG CANCERS

Studies have shown that the risk for bladder cancer increased with decreases in serum levels of both lycopene and selenium. For breast, lung, and cervical cancers, results have been mixed, with some research indicating possible links between lycopene and cervical cancer. The same is true of possible links between lycopene and breast cancer.

CARDIOVASCULAR DISEASES

Lycopene due to its antioxidant properties reduces lipids by inhibiting enzymes involved in cholesterol synthesis and by enhancing LDL degradation.

DIABETES

Intake of fruits and vegetables rich in Carotenoids including lycopene is a protective factor against Lycopene.

AIDS

Several studies have reported reduced concentration of micronutrients including lycopene in patients with HIV infection, despite adequate dietary intake, particularly in those with lower CD4 + cell count.

RECOMMENDED INTAKE LEVELS OF LYCOPENE

Estimating the daily intake of lycopene has been difficult due to the variability of reported values in the food sources. On an average, the daily intake of lycopene is estimated to be 3.7 mg. Based on previously reported studies, a daily intake of 25-30 mg lycopene was initially suggested . However, based on the results of a recent study where absorption of lycopene from tomato ketchup and supplement at the intake levels of 5, 10 and 20 mg daily for one week were evaluated, the suggested daily intake of lycopene was modified to 5-10 mg . This level of intake can easily be achieved by ingesting several dietary sources of lycopene.

LYCOPENE INTAKE IN VARIOUS DISEASES

- 8 mg/ day for treatment of oral leukoplakia.
- 6.5 mg/ day for treatment of lung cancer in non smoking women.
- 12 mg/ day for treatment of lung cancer in non smoking men.
- 6 mg/ day for reducing risk of prostrate cancer.
- 30 mg/ day decrease growth of prostrate cancer.
- 60 mg/ day reduce LDL cholesterol

TOXICITY

No Toxicity till now have been reported.

ADVERSE EFFECT

Lycopenodermia: High intakes of lycopene-rich foods or supplements may result in a deep orange discoloration of the skin known as lycopenodermia. Because lycopene is more

ntensely colored than the carotenes, lycopenodermia may occur at lower doses than carotenodermia.

SUMMARY

Intake of tomatoes and tomato-based products and plasma levels of lycopene have been relatively consistently associated with a lower risk of a variety of diseases. Evidence is strongest for cancers of the lung, stomach, and prostate gland and is suggestive for cancers of the cervix, breast, oral cavity, pancreas, colorectum, and esophagus. A large body of evidence also indicates that other fruits and vegetables may have additional or complementary benefits. These findings add further support to current dietary recommendations to increase consumption of fruits and vegetables to reduce cancer risk. The benefits of tomatoes and tomato products are often attributed to the carotenoid lycopene. However, a direct benefit of lycopene has not been proven, and other compounds in tomatoes alone or interacting with lycopene may be important. It is critical to recognize that the current evidence regarding dietary intake and lycopene blood concentrations reflects consumption of tomatoes and tomato products rather than purified lycopene supplements. The pharmacokinetic properties of lycopene remain poorly understood, and it is premature to recommend use of pharmacologic doses of lycopene for any health benefit. Further research on the bioavailability, pharmacology, and biology of this potentially important carotenoid is clearly warranted. Until more definitive data regarding specific benefits of purified forms of lycopene are available, current

recommendations should emphasize the health benefits of diets rich in a variety of fruits and vegetables, including tomatoes and tomato-based products.

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