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LYCOPENE AND THE ROLE IN METABOLIC PREVENTION

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Abstract

The origin of the tomato plant seems to be South America, in particular Chile and Ecuador, where it grows as a wild plant due to the tropical climate and is able to bear fruit throughout the year, while in European regions, if cultivated in 'open, has a seasonal cycle limited to the summer period. From here, it later spread to Central America and it was the Spaniards who made it known in Europe in the 16th century. Only at the end of the 18th century, the cultivation of tomatoes for food purposes experienced a strong boost in Europe, mainly in France and Southern Italy. Starting from the 19th century, the tomato was finally included in European gastronomic treaties, favoring a conspicuous diffusion both on the tables of the richest and those of the less well-off. Today tomatoes are a staple of our diet a series of researches have identified the effects that the consumption of this particular food, in its many variations, has on our health. If previously the effects that tomatoes have on the improvement of blood lipids were recognized, now researchers have identified a direct correlation between the risk of cardiovascular mortality and the consumption of the fruit, for the presence of Lycopene, a carotenoid antioxidant. It is lycopene, in particular, that produces the greatest benefits for our body. It is a powerful antioxidant that determines, among other things, the particular red color of the tomato. Through research on the effects of a diet rich in tomatoes on the body, the experts found a progressive decrease in the concentration of cholesterol accompanied by a decrease in cardiovascular risk.

Keywords: tomato, cardiovascular risk, antioxidant, diet

Introduction

Oxidative stress is now recognized as an important etiological factor in the causation of several chronic diseases including cancer, cardiovascular diseases, osteoporosis, and diabetes. Antioxidants play an important role in mitigating the damaging effects of oxidative stress on cells. Lycopene, a carotenoid antioxidant, has received considerable scientific interest in recent years. Epidemiological, tissue culture, and animal studies provide convincing evidence supporting the role of lycopene in the prevention of chronic diseases (1). Carotenoids, residues present in fruit and vegetables play an important role in maintaining cellular homeostasis. The dietary need for beta-carotene carotenoid, a precursor of vitamin A, has been recognized for many decades. More recently, among the carotenoids, lycopene has attracted considerable interest among researchers. Lycopene is the red carotenoid found mainly in tomatoes and some fruits and vegetables. It has been observed that it can exert a beneficial action in serious diseases, such as cancer and coronary heart disease as well as in other chronic diseases. (2). These data have been studied extensively, through epidemiological studies, biochemical investigations on the properties of lycopene and the comprehensive examination of its bioavailability in tomato-based diets and human intervention studies are now being conducted to validate epidemiological observations and to understand the mechanisms of action of lycopene in disease prevention. To obtain a better understanding of the role of lycopene in human health, this chapter reviews the most recent information pertaining to its chemistry, bioavailability, metabolism, role in the prevention of prostate cancer and cancer of other target organs, its role in cardiovascular diseases, osteoporosis, hypertension, and male infertility

Fruits and vegetables are a good source of vitamins, minerals and antioxidant compounds in general. This is important since the presence of antioxidants can promote the disposal, mediated by cellular enzymatic systems, of reactive oxygen species (ROS), hydroxide radicals, peroxides or other highly reactive oxygen components (1-3).

These compounds are in fact harmful for cellular metabolism as they convert low-density lipoprotein cholesterol (LDL) into reactive oxidized forms, which are the main risk factor for heart disease. These reactive forms can modify essential enzymes and proteins, but above all they are intermediates capable of inducing mutations in DNA, a fundamental step in the processes of tumor initiation and promotion. It is necessary to emphasize that the formation and presence of radicals can be minimized with antioxidants present in fruit and vegetables, where vegetables seem to be of greater importance (4). However, these foods are not always contained in the traditional Mediterranean Diet.

Infact, the Mediterranean diet is currently considered a healthy dietary pattern. It includes a great variety of foods, which are eaten in moderation and within a positive social environment. The generic term "Mediterranean diet" was born after the "Seven Countries Study" led by Ancel Keys around 1960. This dietary pattern is characterized by a high intake of fruits and vegetables, whole grains, legumes, nuts, fish, white meats and olive oil. It also includes moderate consumption of fermented dairy products, low intake of red meat and drinking wine with moderation during meals. Nutritionally, this diet is low in saturated fats and animal protein, high in antioxidants, fiber and monounsaturated fats, and exhibits an adequate omega-6/omega-3 fatty acid balance. The main bioactive compounds, which explain the health benefits of this dietary pattern, are antioxidants, fiber, monounsaturated and omega-3 fatty acids, phytosterols, probiotics and The traditional intake of tomatoes takes on an important aspect above all for the presence of carotenoids and in particular of lycopene. This diet is not exclusively confined to the Mediterranean Basin and today represents an important strategy for the prevention of metabolic diseases. (5)

Methods

Metabolic syndrome (MS) is a complex pathophysiologic state whose prevalence continues to rise worldwide representing a major and escalating public health problem. Although there is no international consensus to define MS, the

majority of scientific societies contemplate the presence of three of the following five criteria: obesity with excess of abdominal fat evidenced by waist circumference ≥102 cm in men or ≥88 cm in woman, fasting plasma glucose ≥100 mg/dL; blood pressure ≥130/85 mmHg; triglycerides (TG) ≥150 mg/dL; high density lipoprotein cholesterol (HDLc) <40 mg/dL in men or <50 mg/dL.

All forms of lycopene are slightly insoluble in water. In the tomato itself, lycopene is attached to its membrane and is not released very easily. During the cooking of tomatoes, the binding of lycopene to the membrane is weakened and for this reason, cooked tomatoes make large quantities of lycopene available compared to fresh tomatoes. This is also true of the carotene in carrots.

Lycopene is chemically defined as a linear acyclic carotenoid characterized by 11 conjugated double bonds (Fig. 1) but, unlike beta-carotene, in the body it is not transformed into vitamin A.

Lycopene exists in several stereoisomeric forms. Double bonds are subject to isomerization. In nature, lycopene is found in the structural form of "trans" type isomers, however exposure to heat sources or even light irradiation involves a modification of its structure in cis isomers (mainly in position 5, 9, 13, 15), which are more assimilable by the human body and, therefore, show greater bioavailability. It seems that this can also happen in vivo. Lycopene, due to its chemical structure, is a non-polar compound that dissolves much better in oils, such as olive oil. Therefore the Mediterranean nutritional tradition, which is used to consume cooked tomatoes as part of the diet associated with olive oil, not only provides an excellent release of ingested lycopene as part of the total diet, but is also absorbed with olive oil and can reach tissues and cells. Since the human body cannot synthesize carotenoids endogenously, the body satisfies its need for carotenoids only through the diet.

Generally, tomato fruit and tomato-based food products provide at least 85% of lycopene; the remaining 15% is usually obtained from watermelon, grapefruit, guava and papaya. Tomato juice, tomato soup and foods seasoned with tomato sauces are, therefore, the main products that contribute to the intake of lycopene. The absorption of carotenoids from the diet has been studied for many years. Dietary bioavailability of lycopene appears to depend on several factors. It is better absorbed from diets rich in lipids and cooked foods, rather than raw ones (6-10). Once ingested, lycopene appears in plasma, initially in chylomicrons (microscopic emulsified fat particles found in plasma and lymph that come from fat digestion) and very low-density lipoprotein (VLDL) fractions and later in low-fat lipoproteins. density (LDL) and high density (HDL).

The highest levels are present in LDL. Serum concentrations range from approximately 20 - 500 mcg / liter of serum with large variations between individuals. Numerous evidences suggest that LDL modified by oxidation are harmful to the arterial wall and that atherosclerosis can be attenuated by natural antioxidants. As pointed out by Fuhrman (11), lycopene in tomatoes, alone or in conjunction with other natural antioxidants, inhibits the oxidation of LDL. In addition, a dietary supplement of 60 mg / day of tomato lycopene over a period of three months produces a significant reduction in plasma LDL. This is in agreement with in vitro results indicating that lycopene suppresses cholesterol synthesis and increases the LDL receptor activity on macrophages (11).

Recent studies report that higher serum levels of lycopene are associated with longer survival in people with metabolic syndrome and shown to inhibit the proliferation of cancer cells. The rapid and uncontrolled division of cells is a characteristic of the metabolism of cancer cells; the activity of lycopene in delaying the progression of the cell cycle explains its antitumor activity. Furthermore, lycopene can block cell transformation by reducing the loss of contact inhibition of cancer cells (12). Lycopene, in fact, is able to stimulate the production of the protein "connexin 43", one of the main building blocks of "gap-junctions" or intercellular connections Lycopene induces phase II enzymes that help eliminate carcinogens and toxins from the body. It has been suggested that the change in the expression levels of numerous regulatory proteins is related to the ability of lycopene to modulate various transcriptional factors that play a key role in the synthesis of new proteins (13).

Results

Lycopene is an antioxidant found in red fruit and vegetables which, in addition to being used as a food coloring, is also used in the preparation of supplements and functional foods. The study published in Nutrition Research suggests that higher serum levels of lycopene are associated with longer survival in people with metabolic syndrome. This is the first study that analyzed the association between lycopene in serum and the risk of mortality in subjects with this syndrome. The data of 2,499 people with metabolic syndrome were analyzed: the results showed that the survival of people with the highest blood lycopene concentration was about 4 months higher than the group with average serum lycopene levels and about 13 months compared to people with the lowest serum levels.

We know that as a natural antioxidant, lycopene is able to reduce oxidative stress and reduce inflammation. Animal experiments also show that lycopene can statistically significantly reduce the expression of pro-inflammatory cytokines and chemokines. (14) In fact, accumulated evidence suggests that a synergistic effect of various micronutrients, contained in diets rich in fruit and vegetables, may be the basis of disease prevention. Indeed, the sources of lycopene used in most human studies were products prepared from or extracted from tomatoes containing lycopene and other micronutrients from the tomato itself and carotenoids in various proportions. Pure lycopene has not been tested as a single agent in human prevention studies. On the other hand, many studies showing the positive effect of lycopene in alleviating chronic conditions, have been conducted in subjects who have eaten tomato based foods or tomato extracts but not the pure residue. For example, the oleoresin preparation used in many of these studies contained other tomato carotenoids such as phytoene, phytofluene and beta-carotene. In fact, it is possible that the beneficial effects are the result of a synergistic effect of the tomato carotenoids and the other antioxidants present in it (15.16).

A review on the relationship between tomato consumption and cancer was published by Giovannucci et al. (17). It has been reported that there is an inverse proportionality between the intake of tomatoes or the level of plasma lycopene and the risk of cancer at a defined anatomical site. None of the studies cited in this review indicated that high tomato consumption or high plasma levels of lycopene is associated with an increased risk of cancer. The positive effect of lycopene is stronger for cancers of the prostate, lung and stomach. The data are also indicative of a protective effect for cancers of the pancreas, colorectal, esophagus, oral cavity, breast and cervix.

Giovannucci et al. (17) suggest that lycopene may contribute to the beneficial effects of tomato-containing foods, but this has not been proven with conclusive evidence. In addition, as discussed above, the anti-cancer properties can also be explained by the interactions between the different components found in tomatoes. In a meta-analysis published in 2004 (18) they showed that the intake of tomato-based products reduces the risk of prostate cancer. The researchers analyzed 21 studies involving the daily intake of one or more tomatoes, tomato derivatives, or lycopene supplements: the results indicate that tomato products may play a role in the prevention of prostate cancer. However, this effect is modest (11% reduction in cancer risk) and limited to the intake of large quantities of tomatoes.

Furthermore, the preventive effect is slightly greater in subjects who have taken large quantities of cooked tomato products than in those who have made greater use of tomatoes as they are; this is probably due to the bioavailability of lycopene, which is increased following cooking. It has also been reported that there is a low correlation between dietary intake of lycopene and increased plasma concentrations, possibly due to saturation in absorption, these observations suggest the need for further research. to determine the type and quantity of tomato products to establish with certainty their role in the prevention of prostate cancer (19).

Vegetables, in particular tomatoes, have been indicated as compounds that reduce the concentrations of these carcinogens, probably favoring the formation of no longer toxic metabolites starting from C-hydroxy derivatives of heterocyclic amines. These metabolite have also been found in urine as conjugation products of phase two reactions. Lycopene is naturally present as a trans compound but during heating, the energy

promotes the conversion into a cis compound, which is more soluble in lipids and better absorbed in a diet including olive oil or other oils. Some metabolites of lycopene have been isolated, but it would appear that these are for the most part inefficient as antioxidants. There is epidemiological evidence that those who consume vegetables, including cooked tomatoes, have a low risk of several types of chronic diseases, including heart and major cancers, such as lung, breast, ovarian cancer. , intestines and especially the prostate (19).

For many of these cancers, there are guinea pigs available that can be used to study the beneficial role of lycopene and tomato extracts, and other dietary factors such as oils that reduce the incidence of mortality depending on the amount consumed. Furthermore, in the prevention of carcinogenesis, cancer cells can be eliminated through the phenomenon of apoptosis, which could be increased by lycopene. Modern medical science establishes the importance of chemopreventive agents through clinical studies, generally very long and expensive, or through large epidemiological studies worldwide that are aimed at studying the incidence of diseases and mortality in different countries with different nutritional habits. In particular, it was highlighted that in Japan the population has taken on Western habits and this has resulted in a significant increase in cancer cases, including invasive prostate cancer (21) compared the analysis of sections of the prostate of an old Japanese and a Japanese resident of Haway; in the first case it detected a carcinoma in situ, but not completely invasive, unlike the second case, where many more lesions were observed (20).

Finally, Oxidative stress is considered one of the main factors contributing to the risk of cardiovascular disease and cancer. Among the common carotenoids, lycopene is the most powerful antioxidant, according to what has been demonstrated by experimental systems in vitro Based on these studies, the antioxidant potency of carotenoids can be listed as follows:

lycopene> [is greater than] α-tocopherol> α-carotene> β-cryptoxanthin> zeaxanthin> β-carotene> lutein.

The carotenoid blends showed greater efficacy than the single compound. This synergistic effect is most pronounced when lycopene or lutein are present. The increase in the protective activity of the mixtures can be linked to a specific positioning of the different carotenoids in the cell membranes (22-24). Several studies on tomato consumption demonstrate antioxidant properties in humans. For example, it was recently found that the daily intake of 15mg of lycopene, combined with other phytonutrients in tomatoes, significantly increases the protection of lipoproteins from oxidation. These results indicate that lycopene absorbed by tomato products can act as an antioxidant in vivo (25).

Lycopene modulates the mechanisms underlying cell proliferation, the activity of growth factors and intercellular communication through gap junctions (26).

The effect of tomato-derived lycopene on low carotenoids and enhancers systemic inflammation and oxidation it is found in severe obesity

Fat tissue mediates the production of inflammatory cytokines and oxidative production, which are key steps in the development of type 2 diabetes and atherosclerosis. The positive effect of the potent tomato derived antioxidant carotenoids, lycopene, was found on plasma antioxidants (carotenoids and vitamin E) inflammatory markers (C- reactive protein, interleukine-6, tumor necrosis factor-alpha) and oxidation products (conjugated dienes)

The prevalence of obesity (body mass index 30≥ kg/ m2) is steadily growing, with more than 50% in certain populations in Israel, Obesity is strongly correlated with cardiovascular morbidity and mortality. The adipose tissue secretes inflammatory cytokines such as interleukine -6 and tumor necrosis factor –alpha, which contribute to atherosclerosis by inducing insulin resistance and up-regulating the expression of other inflammatory mediators. Cardiovascular morbidity and mortality may decrease by reducing the level of chronic inflammation and oxidative stress. Carotenoids are well-known lipid soluble antioxidants, sourcing mainly from fruit and vegetables. Diets rich in tomato products are associated with decreased risk of chronic diseases. (27)

Discussion

In the light of what emerges and to reduce the risk related to metabolic diseases, the diet should be rich in lycopen. Lycopene abounds in fruits and vegetables, varying in quantities from 30 to 200 mg / kg. Much depends above all on the degree of ripeness of the vegetable and obviously on the choice to eat organic. We find it mainly in red and yellow colored foods. The food that is richer in it is definitely the tomato, but we also find it in carrots and peppers. Daily requirement generally ranges from 50 to 100 mg per day, but thanks to a balanced diet rich in seasonal vegetables and fruit, it can be easily satisfied. Among the fruit we can make the most of it by eating watermelon, pink grapefruit, apricot, grapes, pomegranate, cherries, strawberries and oranges. (28) The researchers found that tomatoes (Lycopersicon esculentum) is termed as "the most popular vegetable fruit, are the biggest source of dietary lycopene, a powerful antioxidant that, unlike nutrients in most fresh fruits and vegetables, has even greater bioavailability after cooking and processing. Tomatoes are widely available, people of all ages and cultures like them, they are cost-effective, and are available in many forms, tomatoes affect nutrition and health benefits (29-30). It is a fruit of good nutritive value as it is fairly rich in vitamins (vitamin C), and other minerals like calcium, phosphorus and iron and he can be included in the daily diet of young and growing children.

Chemical analysis of tomato shows that it contains less purine (11 mg/100 g) than carrots (17 mg), potatoes (16 mg), cabbages (32 mg) and other vegetables. Oxalic acid content of tomato is relatively less than beets, potatoes, cucumber and lettuce. Experts now recommend inclusion of tomatoes in the diets of gall bladder patients.

Dosages of 5 - 60 mg (5,000 mcg - 60,000 mcg) of lycopene per day have been used in studies on this substance. Obviously, if other natural antioxidants are taken in addition to lycopene, such as certain vitamins, lipoic acid or coenzyme Q-10, the beneficial effect on our body increases considerably (31-32). In fact, it has been shown that the antioxidant activity of lycopene benefits from the synergistic relationship with other micronutrients.

It may aggravate gout problems and uric acid diseases.

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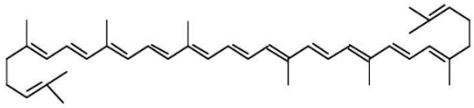

Figure 1: Chemical structure of lycopene

Table 1. *Nutrient composition of tomatoes*

32 calories (kcal)
170.14 g of water
1.58 g of protein
2.2 g of fiber
5.8 g of carbohydrate
0 g cholesterol
18 mg of calcium
427 mg of potassium
43 mg of phosphorus
24.7 mg of vitamin C
1499 international units (IU) of vitamin A