

## HEALTH PROPERTIES OF LYCOPERSICUM ESCULENTUM

Finelli, F.<sup>1\*</sup>; Bonomo, M. G.<sup>2,4\*</sup>; Giuzio, F.<sup>2</sup>; Mang, S.M.<sup>3</sup>; Capasso, A.<sup>5</sup>; Salzano, G.<sup>2,4</sup>; Sinicropi, M.S.<sup>6</sup>; Saturnino, C.<sup>2,4</sup>

<sup>1</sup> *Struttura Complessa UOP-AO "G. Moscati" Avellino, Italy*

<sup>2</sup> *Dipartimento di Scienze, <sup>3</sup> Scuola di Scienze Agrarie, Forestali, Alimentari e Ambientali (SAFE), Università degli Studi della Basilicata, Viale dell'Ateneo Lucano 10, 85100 Potenza, Italy*

<sup>4</sup> *Spinoff TNcKILLERS, Viale dell'Ateneo Lucano 10, 85100 Potenza, Italy*

<sup>5</sup> *Dipartimento di Farmacia, Università degli Studi di Salerno, Via Giovanni Paolo II 132, 84084 Fisciano (SA), Italy*

<sup>6</sup> *Dipartimento di Farmacia e Scienze della Salute e della Nutrizione, Università della Calabria, 87036 Arcavata di Rende, CS, Italy*

[\\*medfinelli@gmail.com](mailto:medfinelli@gmail.com)

[\\*mariagrazia.bonomo@unibas.it](mailto:mariagrazia.bonomo@unibas.it)

### Abstract

The tomato, *Lycopersicon esculentum*, is a horticultural plant belonging to the Solanaceae family. In Italy, the term "tomato" is found for the first time in the famous "Herbarius" by Pietro Mattioli. The etymology of the name leads back to the Latin "pomum aureus", apple or golden apple. Unlike in other languages, such as English, the term "tomato" is linked to the etymology of the Aztec version "Xitotomate". 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 through out 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.

The cultivation of the tomato plant was already widespread in the pre-Columbian age, when it was used as an ornamental plant and was not used in the kitchen: this is because the tomato was considered poisonous due to its high content in solanine, a substance considered harmful for the 'man. In 1544, the Italian herbalist Pietro Mattioli classified the tomato plant among the poisonous species. It is not clear when the tomato, as an ornamental and poisonous plant, was considered edible by Europeans; it should be noted that not even the inhabitants of South America ate the fruits of the plant. From Europe, or perhaps more precisely from Spain, the tomato plant landed in Morocco, where it found an ideal climate, and from there it spread throughout the Mediterranean basin. Starting from the seventeenth century, in southern Europe, as well as in Bohemia and England, the tomato began to be used fresh and for the preparation of sauces, while its diffusion as a food in northern Europe encountered many difficulties, perhaps due to the presence of other similar wild plants which, due to their high alkaloid content, were not suitable for food consumption.

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. There is no shortage of extravagant beliefs and

legends related to the properties of the tomato: in the 1500s and 1600s it was, in fact, attributed aphrodisiac and exciting powers to the point of being used by alchemists of the time in the production of potions and magical filters. It is commonly believed that the tomato has a refreshing, astringent, thirst-quenching, diuretic and digestive action and is rich in nutritional constituents that promote a state of physical well-being.

**Keywords:** *tomato, nourishing, antioxidant, tumor-free*

## Introduction

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. (1). 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.

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 (2). Products such as soy foods and green or black tea are also excellent sources of antioxidant defense that play a protective role in Asia, particularly in Japan, Korea and various parts of China (2-4). However, these foods are not always contained in the traditional Mediterranean Diet. The traditional intake of tomatoes in the Mediterranean region therefore takes on an important aspect above all for the presence of carotenoids and in particular of lycopene.

## Methods

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. 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, 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 (5-9). 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 (10), 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 (10).

Lycopene has been found in most human tissues but does not accumulate uniformly (11). Accumulation occurs preferentially in the adrenal glands and testicles. The main objective of diets that aim to obtain an improvement in health is, among many, precisely to increase the levels of lycopene in the tissues. Little is known about the metabolism or degradation of lycopene in mammals. A number of oxidized metabolites have been found in plasma and tissues, but further studies are needed to evaluate their possible physiological role (11-13). Research has indicated that lycopene may exert beneficial effects on human health, while not being an essential compound. As a carotenoid, lycopene protects lipids, proteins and DNA from oxidative damage. It is a powerful inactivator of oxygen in the singlet state (a reactive form of oxygen), which suggests that it may have comparatively stronger antioxidant properties than the other carotenoids normally present in plasma (14-16).

Lycopene has been 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 (16).

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 (17).

### Results

It has been highlighted that the use of a single carotenoid, or any other micronutrient that has shown positive results in in vitro models and on animals, is not sufficient alone to determine the same effects on humans. 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 (18-19). In order to ascertain the contribution of each tomato component in determining these effects, a study compared the activity of whole freeze-dried tomatoes (tomato powder) or pure lycopene in a rat prostate cancer model (15).

The rats were treated with the carcinogen NMU (N-methyl-N-nitrosourea) and with androgens to stimulate prostate carcinogenesis and the ability of these two preparations to reduce mortality due to prostate cancer was compared; the latter was 25% lower for rats fed with freeze-dried tomato than in

the control group, whereas mortality from prostate cancer of rats fed with pure lycopene was similar to that of the control group. These results show that the consumption of tomato powder, but not pure lycopene, increases survival in rats with prostate cancer suggesting that tomato products contain other residues, in addition to lycopene, which can improve disease prognosis (15). A review on the relationship between tomato consumption and cancer was published by Giovannucci et al. (16). 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. (16) 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 (17) 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 (17).

Prostate cancer is the third leading cause of death worldwide. In the United States, prostate cancer is second only to lung cancer in incidence and cause of death; in particular in the United States it is possible to find differences between races, as black men show a higher probability of death than whites; the reason for this difference based on race is not yet clear but it also seems to be linked to the quantity of dairy products consumed in the diet (19).

A recent article reports low serum levels of lycopene in blacks correlated, at the epidemiological level, with a high rate of prostate cancer in these subjects (20). In the Mediterranean people, a high intake of vegetables and, especially of cooked tomatoes, reduces the incidence of prostate cancer, probably as a result of two-level activity. The first concerns probable carcinogens and genotoxic agents such as heterocyclic amines, formed during the cooking of meat, especially veal and pork. In the Mediterranean region, red meats are widely used in food and cooking is often done by adding a liquid to marinate that allows the meat not to oxidize, eliminating, or at least decreasing, the formation of carcinogenic compounds such as heterocyclic amines. The second level concerns the types of oils used, which are normally represented by olive oil. It has been shown that individuals who consume well-cooked meat have traces of heterocyclic amines in their urine (21).

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 metabolites 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 Hawaii; 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).

This work led to the conclusion that carcinogens are similar in traditional Japan as in the United States; in the first case they come, perhaps, from exposure to heterocyclic amines produced during the frying of fish. Regular eating habits in Japan were low in fat but high in vegetables, fruit, soy, and green tea. With the development of Westernization, there is an increase in the incidence of invasive prostate cancer. The same is happening in Italy, especially in the north where we are witnessing an affirmation of American dietetic habits, facilitated by the expansion of fast food / restaurants: very few quantities of protective vegetables, including tomatoes, are consumed. In the USA, the federal government guarantees an economic contribution to farmers to maintain and increase the production of certain foods. It would be desirable to extend these forms of economic support also to fruit and vegetables, including tomatoes, because this would allow to keep the market price of these products

substantially low and the consumer could easily buy them and include them in their diet without limitations (21).

People who need medical care and treatment of illnesses require high costs. Therefore, having foods that prevent further damage, at low cost, would be an excellent investment.

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]  $\alpha$ -tocopherol >  $\alpha$ -carotene >  $\beta$ -cryptoxanthin > zeaxanthin >  $\beta$ -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 has been found to inhibit the proliferation of numerous types of cancerous cells, including those of the breast, prostate, lung and endometrium. The inhibitory mechanism is probably related not to induction of apoptosis, nor to necrosis for diseased cells, but to inhibition of cell cycle progression from G<sub>0</sub> / G<sub>1</sub> to S phase. Inhibition of cell proliferation is correlated with a decrease in the levels of the cyclin D1 protein, a key regulator of this process. Cyclin D1 is known for its ability to regulate the cell cycle and therefore proliferation, it can be rightly considered an oncogene (gene whose dysregulation causes normal cells to become cancerous) often over-expressed in many cell lines of breast cancer as well as in primary cancers (25).

The stimulation of the growth of breast cancer cells by the type 1 insulin growth factor (IGF-1) is significantly reduced by the physiological concentrations of lycopene in experimental studies conducted in vitro (26). The importance of this discovery in cancer prevention is linked to epidemiological results which found that the increase in IGF-1 levels corresponds to a relative increase in the risk of breast and prostate cancer (27). If lycopene's interference with IGF-1 stimulation in the development of cancer cells is confirmed by clinical studies, this would provide a rationale for promoting increased lycopene intake, especially through tomato-based food products, for cancer prevention. Induction of phase II enzymes, which conjugate reactive electrophiles and act as indirect antioxidants, also appears to be an effective strategy for achieving protection against various carcinogens in both animals and humans.

One study associated the chemopreventive effect of lycopene with a reduction in the incidence of tumors in the oral mucosa. In particular, the frequency of dimethyl benzene-anthracene-induced tumors (DMBA) in the hamster was lower in the lycopene-treated group than in the control group consisting of hamsters treated only with the chemical carcinogen DMBA, and this reduction is associated with an increase simultaneous with reduced glutathione levels and glutathione S-transferase (GST) - an enzyme of the glutathione redox cycle. These results suggest that lycopene-induced increase in GSH and phase II GST enzyme levels inactivates carcinogens through conjugation reactions.

Lycopene modulates the mechanisms underlying cell proliferation, the activity of growth factors and intercellular communication through gap junctions (28). In addition, lycopene produces changes in the expression of many proteins that participate in these processes such as connexins, cyclins and phase II enzymes. Consequently, one may wonder by what mechanisms lycopene is able to affect so many different cellular pathways. The change in the expression of multiple proteins suggests that the initial action of lycopene involves the regulation of transcription (29). Transcription is the process by which the genetic information carried by the DNA is

converted into RNA which acts as a messenger. This biochemical step leads to the formation of new proteins through the process called translation. This may be due to a direct interaction of carotenoid molecules or their derivatives with transcription factors, for example, with ligand-activated nuclear receptors or indirect changes in transcriptional activity, through changes in the cellular redox state, involving the redox-sensitive transcription system (30).

### Discussion

The researchers found that tomatoes 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 (31-32) Tomato (*Lycopersicon esculentum*) is termed as "the most popular vegetable fruit. 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.

It has been confirmed that tomato and tomato sauce lower blood pressure and the risk of heart disease. Effectiveness of tomatoes in lowering blood pressure is attributed to lycopene, a chemical present in tomato. 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. It may aggravate gout problems and uric acid diseases. In fact, tomato is included in the diet as it has uric acid lowering effect. moreover, the tomato is also included in ketogenic diets. Low in fat but also carbs (with just 2.4 g of net carbs per ½ cup), tomatoes are also keto-friendly. The same serving size of tomatoes contains 2.4 g of sugar and 16 calories.

## References

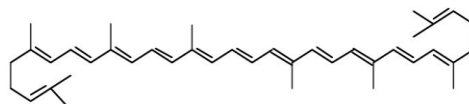
1. Marnett, L. J. (2001). Oxyradicals and DNA damage. *Carcinogenesis*, 21, 361-370.
2. La Vecchia, C., & Tavani, A. (1998). Fruit and vegetables, and human cancer. *European Journal of Cancer Prevention*, 7, 3-8.
3. Tommonaro, G., Caporale, A., De Martino, L., Popolo, A., De Prisco, R., Nicolaus, B., Abbamondi, G.R., & Saturnino, C. (2014). Antioxidant and cytotoxic activities investigation of tomato seed extracts. *Natural Product Research*, 28, 764-768.
4. Sofo, A., Elshafie, H.S., Scopa, A., Mang, S.M., & Camele, I. (2018). Impact of airborne zinc pollution on the antimicrobial activity of olive oil and the microbial metabolic profiles of Zn-contaminated soils in an Italian olive orchard. *Journal of Trace Elements in Medicine and Biology*, 49, 276-284.
5. Strazzullo, G., De Giulio, A., Tommonaro, G., La Pastina, C., Poli, A., Nicolaus, B., De Prisco, R., & Saturnino, C. (2007). Antioxidative Activity and Lycopene and beta-carotene contents in different cultivars of Tomato (*Lycopersicon esculentum*). *International Journal of Food Properties*, 10, 1-9.
6. Saturnino, C., Spagnuolo, A., Palladino, C., Popolo, A., Tommonaro, G., De Prisco, R., & Pinto, A. (2013). Antiproliferative Activity of "Lycopersicon esculentum" Leaves (Var. Paul Robenson): Preliminary Study. *Food Science and Nutrition*, 4, 632-635.
7. Tommonaro, G., Prisco, R., Abbamondi, G.R., Marzocco, S., Saturnino, C., Poli, A., & Nicolaus, B. (2012). Evaluation of antioxidant properties, total phenolic content, and biological activities of new tomato hybrids of industrial interest. *Journal of Medicinal Food*, 15(5):483-4
8. Bohm, V., & Bitsch, R. (1999). Intestinal absorption of lycopene from different matrices and interactions to other carotenoids, the lipid status, and the antioxidant capacity of human plasma. *European Journal of Nutrition*, 38(3), 118-125.
9. Cafaro, C., Bonomo, M.G., Guerrieri, A., Crispo, F., Ciriello, R., & Salzano, G. (2016). Assessment of the genetic polymorphism and physiological characterization of indigenous *Oenococcus oeni* strains isolated from Aglianico del Vulture red wine. *Folia Microbiologica*, 61, 1-10.
10. Fuhrman, B., Ben-Yaish, L., Attias, J., Hayek, T., & Aviram, M. (1997). Tomato lycopene and beta-carotene inhibit low density lipoprotein oxidation and this effect depends on lipoprotein vitamin E content. *Nutrition Metabolism & Cardiovascular Diseases*, 7, 433-443.
11. Khachik, F., Carvalho, L., Bemstein, P.S., Muir, G.J., Zhao, D.Y., & Katz, N.B. (2002). Chemistry, distribution, and metabolism of tomato carotenoids and their impact on human health. *Experimental Biology and Medicine*, 227(10), 845-851.
12. Mang, S.M., Racioppi, R., Camele, I., Rana, G.L., & D'Auria, M. (2015). Use of volatile metabolite profiles to distinguish three *Monilinia* species. *Journal of Plant Pathology*, 97, 55-59.
13. Autore, G., Caruso, A., Marzocco, S., Nicolaus, B., Palladino, C., Pinto, A., Popolo, A., Sinicropi, M.S., Tommonaro, G., & Saturnino, C. (2010). Acetamide derivatives with antioxidant activity and potential anti-inflammatory activity. *Molecules*, 15, 2028-2038.
14. Amir, H., Karas, M., Giat, J. (1999). Lycopene and 1,25-dihydroxyvitamin-D<sub>3</sub> cooperate in the inhibition of cell cycle progression and induction of differentiation in HL-60 leukemic cells. *Nutrition and Cancer*, 33, 105-112.
15. Boileau, T.W., Liao, Z., Kim, S., Lemeshow, S., Erdman, J.W. Jr, & Clinton, S.K. (2003). Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. *Journal of the National Cancer Institute*, 95(21), 1578-1586.
16. Giovannucci, E. (1999). Tomatoes, tomato-based products, lycopene, and cancer: review of the epidemiologic literature.



- Journal of the National Cancer Institute*, 91, 317-331.
17. Etminan, M., Takkouche, B., & Caamano-Isorna, F. (2004). The role of tomato products and lycopene in the prevention of prostate cancer: a meta-analysis of observational studies. *Cancer Epidemiology, Biomarkers & Prevention*, 13(3), 340-345.
  18. Freeman, V.L., Meydani, M., & Yong, S. (2000). Prostatic levels of tocopherols, carotenoids, and retinol in relation to plasma levels and self-reported usual dietary intake. *American Journal of Epidemiology*, 151(2), 109-118.
  19. Bilton, R., Gerber, M., Grolier, P., & Leoni, C. (2001) Eds. *The White Book on the Antioxidants in tomatoes and Tomato Products and Their Health Benefits*. Avignon, France (End:Suppl. Tomato News) CMITI.
  20. Akazaki, K., & Stemmerman, G.N. (1973). Comparative study of latent carcinoma of the prostate among Japanese in Japan and Hawaii. *Journal of the National Cancer Institute*, 50(5), 1137-1144.
  21. Rimer, B.K. (2000). Cancer control research 2001. *Cancer Causes Control*, 11, 257-270.
  22. Paesano, N., Marzocco, S., Vicidomini, C., Satumino, C., Autore, G., De martino, G., & Sbardella, G. (2005). Synthesis and biological evaluation of 3-benzyl-1-methyl- and 1-methyl-3-phenyl-isothiouras as potential inhibitors of iNOS. *Bioorganic & Medicinal Chemistry Letters*, 15, 539-543.
  23. Greenlee, R.T., Hill-Harmon, M.B., Murray, T., & Thun, M. (2001). Cancer Statistics. *CA Cancer Journal Clinic*, 51, 15-36.
  24. Bonomo, M.G., Cafaro, C., Guerrieri, G., Crispo, F., Milella, L., Calabrone, L., & Salzano, G. (2017). Flow cytometry and capillary electrophoresis analyses in ethanol-stressed *Oenococcus oeni* strains and changes assessment of membrane fatty acids composition. *Journal of Applied Microbiology*, 122 (6), 1615-1626.
  25. Vogt, T.M., Mayne, S.T., Graubard, B.I., Swanson, C.A., Sowell, A.L., Schoenberg, J.B., Swanson, G.M., Greenberg, R.S., Hoover, R.N., Hayes, R.B., & Ziegler, R.G. (2002). Serum lycopene, other serum carotenoids, and risk of prostate cancer in US Blacks and Whites. *American Journal of Epidemiology*, 155, 1023-1032.
  26. Weisburger, J.H. (2002). Comments on the history and importance of aromatic and heterocyclic amines in public health. *Mutation Research*, 506-507.
  27. Karas, M., Amir, H., & Fishman, D. (2000). Lycopene interferes with cell cycle progression and insulin-like growth factor I signaling in mammary cancer cells. *Nutrition & Cancer*, 36, 101-111.
  28. Aust, O., Ale-Agha, N., Zhang, L., Wollersen, H., Sies, H., & Stahl, W. (2003). Lycopene Oxidation Product Enhances Gap Junctional Communication. *Food and Chemical Toxicology*, 41(10), 1399-1407.
  29. Stahl, W., Junghans, A., deBoer, B., Driomina, E.S., Briviba, K., & Sies, H. (1998). Carotenoid mixtures protect multilamellar liposomes against oxidative damage: synergistic effects of lycopene and lutein. *FEBS Letters*, 427(2), 305-308.
  30. Hadley, C.W., Clinton, S.K., & Schwartz, S.J. (2003). The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidative damage. *Journal of Nutrition*, 133(3), 727-732.
  31. Filosa, R., Peduto, A., de Caprariis, P., Satumino, C., Festa, M., Petrella, A., Pau, A., Aime' Pinna, G., La Colla, P., Busonera, B., & Loddo, R. (2007). Synthesis and antiproliferative properties of N3/8-disubstituted 3,8-diazabicyclo[3.2.1]octane analogues of 3,8-bis[2-(3,4,5-trimethoxyphenyl)pyridin-4-yl]methylpiperazine. *European Journal of Medicinal Chemistry*, 42, 293-306.
  32. Canene-Adams, K., Campbell, J.K., Zaripheh, S., Jeffery, E.H., & Erdman J.W.Jr. (2005). The Tomato As a Functional Food. *Journal of Nutrition*, 135, 1226-1230.

**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

**Figure 1.** Chemical structure of lycopene