TOMATO ANTIOXIDANTS AND IT’S DERIVATES.
BENEFITS FOR HEALTH.

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Introduction
Several epidemiological studies suggest that the consumption of fruit and vegetables would be beneficial to human health by reducing the risk of developing cancer and cardio-vascular diseases. However, this protective aspect is more difficult to estimate when one particular group of vegetables or one particular family of nutrients or micro-nutrients is considered.

Recently a great deal of attention has been focused on the tomato and its products. Studies from Giovannucci et al. (1995) and Franceschi et al. (1994) reported that the consumption of tomatoes, tomato sauce and pizza was associated with a reduced risk of developing digestive tract and prostate cancers. Tomatoes are also one of the main part of the Mediterranean diet which has been associated with a low mortality from cardio-vascular troubles. Because tomatoes constitute the almost exclusive source of lycopene, this pigment could be one of the active agents of this protection.

Experimental studies reported that lycopene exhibited antioxidant activities, suppressed cell proliferation and interfered with the growth cancer cells. However, tomatoes are also rich sources of the essential nutrients vitamin C, potassium and folic acid, as well as beta-carotene, gamma-carotene, phytoene, selenium, flavonoids and phenolic acids which may exhibit antioxidant, immunostimulant, photoprotector or even chemopreventive activities on in vitro and animal models. In consequence, several of these constituents would contribute to the disease-preventive properties. However, the following information will focus on lycopene, the more specific antioxidant in tomatoes.

Intakes and tomato composition
In the United States, about 29% of daily lycopene intakes (0.5-5 mg/day) come from tomato sauces, 12% from ketchup, 8% from juice, 8% from pizzas (total from processing tomato products: 57%) and only 12% from fresh tomatoes.

Composition tables show that the tomato (Lycopersicon esculentum) contains 93-95% water and low levels of solid matter. Tomatoes are relatively rich in antioxidants: vitamin C (160-240 mg/kg), provitaminic A carotenes (6-9 mg/kg) and phenolic compounds, flavonoids (5-50 mg/kg) and phenolic acids (10-50
mg/kg). Also present in small quantities are vitamin E (5-20 mg/kg), flavonoids (5-50 mg/kg) and trace elements such as copper (0.1-0.9 mg/kg), manganese (1-1.5 mg/kg) and zinc (1-2.4 mg/kg) which are present in several antioxidant enzymes. Most often the tomato variety is not indicated and the reported values are a mean concentration of the constituents in tomatoes found in local markets. In addition, tables contain values for the whole fruit but heterogeneous distribution of the compounds may occur in the fruit. Thus, antioxidant intakes may be different if skin or seeds are discarded. Hence, the “Campbell 146” variety was shown to contain 4 and 59 mg/kg whole fruit of \(-\text{carotene}\) and lycopene respectively. But the concentration of \(-\text{carotene}\) was 4-fold higher in the locular cavity than in the pericarp whereas the concentration of lycopene was 2-fold higher in the pericarp than in the locular cavity. Flavonoids and phenolic acids also seem more concentrated in the skin than in the flesh and vitamin E appears specifically located in seeds.

**Metabolism**

The carotenoids are insoluble within the aqueous environment of the GI tract and therefore to be absorbed by the body they must be released from the food matrix and solubilised within a lipophilic pool. Within the gastric environment the principal pool is the lipid ingested within the meal. During digestion, carotenoids are transferred from food matrix to mixed micelles. Release from the food matrix is enhanced by efficient particle breakup of the food material either by separation of the plant cells or by their complete disruption. Heating of foods prior to ingestion can also improve carotenoid availability as a result of the dissociation of the protein-carotenoid complexes or dispersion of the crystalline aggregates.

Similarly, if the solubilisation of the carotenoid within a lipid phase is allowed to occur during processing, for example by heating tomato juice with supplemental lipid then the measured absorption of lycopene is enhanced.

Carotenoids are passively absorbed from the micellar phase. However, it is not known if all the carotenoids present in a mixed micelle is absorbed, or whether some is left behind in association with unabsorbed bile salts and cholesterol, perhaps to be absorbed more distally or lost to the large intestine. Factors that increase the thickness of the unstirred layer on the surface of the gut, for example soluble dietary fibre, act as a barrier to the absorption of dietary fats and may, therefore, also inhibit the absorption of carotenoids. Various types of dietary fibre were found to reduce the bioavailability of carotenoids in foods. Matrix effects were proposed as an explanation for the lack of improvement in vitamin A status in Indonesian women fed green leaf vegetables compared with a manufactured wafer containing a similar amount of carotene in oil solution.

The absorbed carotenoids are transported through the enterocyte from the luminal side to the serosal side, where they are re-excreted in chylomicrons into the thoracic duct and hence find their way into the circulating blood. The cleavage of some of the retinol precursor carotenoids by 15, 15’ dioxygenase occurs in the enterocyte. The resulting retinal is reduced to retinol and subsequently esterified to the retinyl ester which also enters the mesenteric lymph with the chylomicrons. The chylomicron remnants, including residual carotenoids, are then cleared from the circulation by passage through the liver. The liver re-exports lipids in the form of very low density lipoproteins (VLDL) and these contain carotenoids dissolved in the lipid portion.

The hydroxy carotenoids (lutein, zeaxanthin) are found almost equally distributed between the LDL and the high density lipoproteins (HDL) in fasting subjects whereas more than 80% of carotene (\(-\text{carotene},\) lycopene) are distributed in VLDL.

**Biological activities**

In addition to the provitamin A activity, carotenoids can also exhibit important biological properties such as antioxidant, immuno activator and anticarcinogenic activities.
In plants carotenoids play a role in helping to quench and prevent the formation of Reactive Oxygen Species (ROS), especially singlet oxygen that is formed during photosynthesis. The importance of this interaction in healthy animals is uncertain. However, singlet oxygen can be formed during the process of lipid peroxidation, and it has also been suggested by Tatsuzawa (1999) that singlet oxygen is also produced during the activation of neutrophils. Singlet oxygen quenching by carotenoids occurs via physical or chemical mechanisms. Isomerisation of the carotenoid may occur during this process. The quenching activity will largely depend upon the number of conjugated double bonds and is influenced to a lesser extent by acyclic or cyclic end-groups. Lycopene has 11 conjugated and 2 non-conjugated double bonds, and is one of the most efficient singlet oxygen quenchers (100 more active than vitamin E).

Carotenoids were shown to interact with free radicals by one electron transfer (formation of a carotenoid cation radical) or by addition reactions. Hence, concerning the first type of reaction (NO\(^{+}\) and ATBS\(^{+}\) scavenging), lycopene was clearly more efficient than \(-\)carotene and xanthophylls. At the opposite, xanthophylls were shown to scavenge peroxyl radicals (free radical adduct) more efficiently than did carotene.

Several studies have suggested that lycopene cation radical might be reduced and thus regenerated by vitamin C and vitamin E. At the opposite, lycopene was shown to quench efficiently xanthophyll radicals. Then this raises the possibility of a synergistic activity between the carotenoids and the more polar xanthophylls present, prior to the interaction with tocopherol. Indeed Stahl (1998) indicated that an antioxidant synergism between lycopene and lutein exists when multilamellar liposomes were oxidised using AMVN.

The potential prooxidant effects of the carotenoids depends upon the formation of carotenoid peroxyl radical. This specie is easily formed as carbon centred radical and usually very stable due to extensive delocalisation of electrons within the polyene structure. This radical will interact with oxygen to form the peroxyl radical. Alternatively the carotenoid may interact with a lipid peroxyl radical to form a carotenoid radical adduct. This may then go on to react with molecular oxygen to form reactive peroxyl radical. This prooxidant effect is dependent upon several factors such as oxygen partial pressure, concentration of the carotenoid, synergism with other antioxidants. In vitro studies indicate that at low oxygen tensions, carotenoids behave as a chain breaking antioxidants whilst at higher tensions they exhibit prooxidant behaviour.

Gap junctions are small, narrow hydrophilic pores connecting the cytosol of adjacent cells. These pores allow the intracellular transport of small molecules (<1000 Da). This enables the transfer of nutrients and ions, the transfer of electrical signals and the promotion of effective cell signalling in tissues. Tumour promoters such as the phorbol esters activate protein kinase C and this subsequently causes a decrease in the expression of Gap junctions. In contrast carotenoids and retinoids induce the expression of gap junctions. It has been noted that natural and synthetic carotenoids bearing a five or six-membered ring system promote an increase in the expression of Gap junctions, whereas open chain polyene compounds had no significant effect upon Gap junction expression. This property was not related to vitamin A activity nor to antioxidant activity.

The effects of carotenoids on the immune response are quite heterogenous and require more investigations.

**Health benefits**

All these data support the hypothesis that carotenoids could be involved in the prevention of degenerative diseases. Such hypothesis was tested through epidemiological studies. Most studies on the protective effect of tomatoes on cancers of the upper aero-digestive tract, as well as lung and stomach have suggested that subjects with high intake, or high plasma concentration of common antioxidants, namely \(-\)carotene
and vitamin C exhibit a lower risk of cancers of aero-digestive tract, as well as lung and stomach. However, lycopene, the specific carotenoid of tomato, was not associated to these cancer sites in six studies out of 8. Although the difficulty in assessing lycopene intake and plasma concentrations has to be kept in mind, these observations suggest that it is not lycopene which is responsible for the protective effect of tomato against upper aero-digestive tract, as well as lung and stomach cancers, but the other compounds present in tomatoes, -carotene and vitamin C, and possibly phenolics. These compounds might act additively or synergistically. Thus, it is the food as a whole which is most likely to be protective, and this may be extended to food habits or typology.

So far, no effect of tomatoes on other cancers has been demonstrated except for the suggestion of a protective effect of cooked tomatoes against prostate cancer. This suggests a role for lycopene since cooking and processing tomatoes concentrates lycopene and makes it more absorbable, whereas vitamin C is decreased in cooked and processed tomatoes. Again, in five studies investigating the relationship of lycopene and prostate cancer, two showed a risk reduction for prostate cancer, especially in aggressive cases.

Fruit and vegetable consumption was shown to be associated with a strong protective effect against stroke and a weaker protective effect against coronary heart disease. Concerning the studies of dietary intake, only one included tomato. In this study, significant correlations were obtained for carrots/squash and salads/green vegetables, but no correlation was obtained for tomatoes.

As part of a European multicentre case-control study on antioxidants (EURAMIC), carotenoids were measured in adipose tissue in 683 individuals with non fatal myocardial infarction (MI) and 727 controls. A borderline significant decreased risk of intima media thickness was observed in the ARIC study based on lycopene plasma concentration after adjustment for all confusion factors. An inverse association was found between carotenoids and MI. After adjustment for age, body mass index, socioeconomic status, smoking, hypertension, and maternal and paternal history of disease, lycopene remained independently protective, with an odd ratio of 0.52 for the contrast of the 10th and 90th percentiles. Lycopene, or some substance highly correlated which is in a common food source, may contribute to the protective effect of vegetable consumption on myocardial infarction risk.

Similarly, in a multicentric ecological study, Bobak et al., (1999) reported that plasma carotenoids including lycopene were inversely related to the coronary heart disease mortality rates. In contrast, in the Street et al.,’s study, (1994), based on the determination of carotenoids concentrations in the sera of patients with MI and controls, no association was observed with lycopene level. Thus to date studies are insufficient to conclude that lycopene is protective against cardiovascular diseases.

In conclusion, we can assume that tomatoes contain several antioxidant micronutrients (vitamin C, polyphenols, carotenoids) with lycopene as the more characteristic of the fruit. Lycopene was shown to induce gap junction between cells and to significantly quench singlet oxygen and scavenge free radical through one electron transfer reaction. Whether lycopene is involved in prevention of cancers and cardiovascular diseases is still unclear and further studies are required.

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