

Bioavailability of Lycopene from Tomato Products

– Review –

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Abstract

Tomatoes and tomato products are the major source of lycopene in the diet. The bioavailability of lycopene is different in raw tomatoes compared to processed tomato products. This is due to the chemical and physical properties of the different lycopene isomers. All-*trans*-lycopene is found in raw tomatoes and is a poor bioavailable source, whereas, processed tomato products are more bioavailable because they contain more *cis*-isomers. Heat and mechanical processing of tomatoes induces rupture of the cell walls, thereby releasing lycopene from its food matrix. Heat processing also induces *cis-trans* isomerization and disrupts protein-carotenoid complexes. Many dietary components also impact lycopene bioavailability, like the amount and type of fat present with the intake and processing of tomato products, the amount and type of fiber present, and the interaction between carotenoids. Fundamentally, anything that enhances formation and incorporation of lycopene in bile acid micelles increases bioavailability, and the opposite is true in that anything that interferes with micelle formation decreases bioavailability.

Key words: bioavailability, carotenoid, health benefit, isomer, lycopene, tomato

INTRODUCTION

Lycopene is an unsaturated hydrocarbon carotenoid containing 13 carbon-carbon double bonds, 11 of which are conjugated and arranged in a linear array. It is one of approximately 600 carotenoids, and a natural pigment synthesized in plants and microorganisms. It is responsible for the bright red color in food such as tomatoes, watermelon, pink grapefruit, and guava (1-4). Unlike β -carotene, lycopene has no provitamin A activity (5,6). Lycopene is found in the highest concentration in tomatoes and tomato products (1,2,7). Lycopene is synthesized by phytoene, a colourless carotene, through series of desaturation reactions in the plant plasmid (1,8). Lycopene consists of *trans*- and *cis*-isomer forms. The all-*trans*-isomer is found in high amounts in fresh tomatoes, whereas *cis*-isomers are found at higher levels in processed tomato products, such as sauce, juice and ketchup (1,3,9,10). *Cis*- and *trans*-isomers have different bioavailabilities in the human blood and tissues due to their chemical and physical properties. Bioavailability is defined as "the fraction of an ingested nutrient that is

available to the body for utilization in normal physiological functions or for storage" (11). There have been numerous studies on the health effects and bioavailability of the carotenoids, such as β -carotene, and over the past years studies on the effects of lycopene have been rapidly growing. Heat processing and homogenization of the food matrix of the tomato enhances the levels of *cis*-lycopene, which is the most bioavailable form in the human body. *Cis*-lycopene is thought to be more bioavailable to the tissue because it is more readily taken up by micelles and chylomicrons for transport, whereas all-*trans* lycopene aggregates within the intestine to form crystals, thereby reducing micellar uptake (5,12).

Lycopene is a powerful antioxidant, and the most efficient quencher of singlet oxygen among the carotenoids. Lycopene has great potential in preventing several chronic diseases, such as cardiovascular disease and certain cancers, like prostate cancer (1,3,6,13-21). The number of conjugated double bonds determines the antioxidant activity of carotenoids, making lycopene a more effective singlet oxygen quencher than β -carotene, as it contains a higher number of double bonds (22). The Med-

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iterranean Diet is considered to be one of the best diets with respect to low mortality from cardiovascular disease and cancers (17,18). This is thought to be due partly to their high intake of tomato and tomato products. This has been demonstrated a great deal in epidemiological studies (17). Both physical and chemical properties are the basis behind their antioxidant actions, including the ability to absorb light and change *cis-trans*-configuration, accepting energy from excited species that serves to protect the plant from light, lipid solubility, and its ability to react with free radicals (20). There are many factors that influence the bioavailability of lycopene including release from the food matrix, lipid, fiber, and carotenoid interaction.

LYCOPENE BIOAVAILABILITY PROCESS IN THE HUMAN BODY

There is still a great deal of speculation about the role of the gastrointestinal system in the bioavailability of lycopene. *Cis*-lycopene isomers, mainly 5-, 9-, 13-, and 15-*cis* lycopene, constitute >50% of total lycopene found in human and animal tissues (5,9,16,23). Raw tomatoes consist of 80~97% of all-*trans* lycopene, therefore the need to convert into *cis*-forms that are better bioavailable to tissues, is of great importance (5,6,15,16). The Canadian dietary intake of lycopene is currently approximately 25.2 mg/day (24). There is currently no recom-

mended daily intake value available for lycopene. Lycopene consists of 21~43% of total carotenoids in the plasma, with levels in the range of 0.22 to 1.06 nmol/mL (3). The absorption of carotenoids first involves the release of lycopene from its food matrix. Micelles are then formed from dietary fatty acids and bile acids. Uptake of lycopene occurs by passive diffusion in the intestinal mucosal cells where it is incorporated into chylomicrons, as phospholipids and triglycerides, mainly LDL and VLDL (4,12,15,25,26). These chylomicrons then distribute lycopene to the tissues and plasma through the lymphatic system (4,15,25,26). The absorption of carotenoids involves many steps that will be discussed further in this review. An outline is shown in Fig. 1 (23).

Selective transport of lycopene to various tissues occurs passively. The adrenals, kidneys, adipose and prostate have been shown to have high levels of lycopene. This is a reason why lycopene is advocated in prostate cancer prevention. Changes in plasma lycopene levels occur rapidly after ingestion of tomato products. However, the level of intake of lycopene does not linearly resemble the increase in plasma lycopene level. Additionally, plasma lycopene levels do not equal the amount absorbed in the tissue. This is due to regulatory mechanisms that are in place that limit mucosal cell uptake and transport (5,23,27). Therefore, the amount that reaches the target tissue should be measured to determine

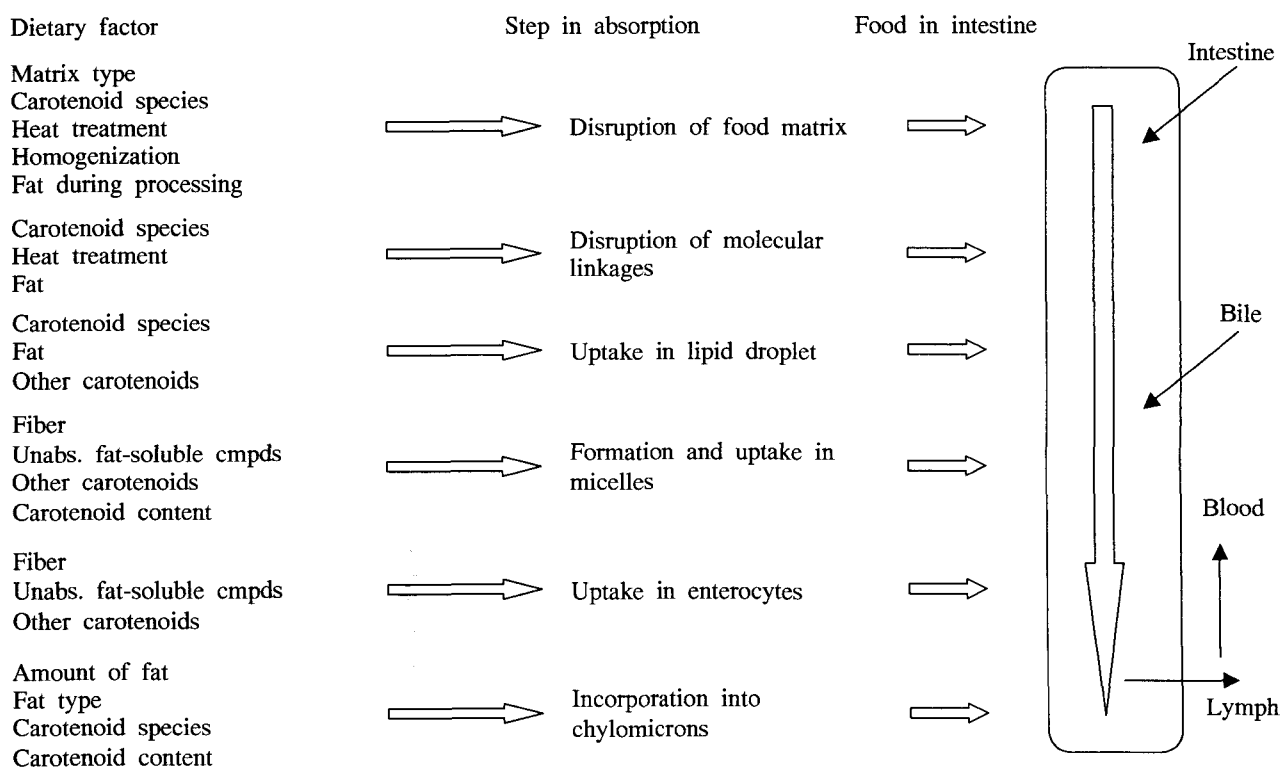


Fig. 1. Schematic diagram of the absorption of carotenoids and dietary factors that affect absorption (23).

bioavailability (28). However, it is often difficult to measure tissue levels due to the invasiveness of the procedure, therefore plasma levels are often adequate in determining bioavailability.

The stomach is thought to have a small role in the isomerization of all-*trans* lycopene to the *cis*-forms. Re et al. (10) performed *in vitro* incubations of tomato puree and lycopene capsules in gastric juices. They found that levels of *cis*-lycopene increased after incubation with gastric juices. This is seen in Fig. 2, which shows the changes in *cis*-lycopene levels after incubation in water and simulated gastric juices.

The hypothesis behind this finding is that the low pH of stomach gastric juice increases the release of lycopene from the food matrix, as well causes *cis-trans* isomerization (5,29). It was previously reported that lipid soluble vitamins were better absorbed in an acidic environment. High hydrogen ion concentrations are thought to reduce the negative surface charge on the micelle and the luminal cell surface, thereby facilitating the absorption of micelles (10). This hypothesis is greatly challenged by the findings of Tyssandier et al. (29), who found that *cis-trans* isomerization would have to occur in a stomach pH of 1.6, which is only found in the fasting state. Although there may be little significant increase in *cis-trans* isomerization of lycopene during digestion, stomach acid may possibly initiate isomerization, as well as releasing lycopene from the food matrix (10,28).

EFFECT OF TRANS AND CIS-ISOMER FORM

Lycopene is found in human tissues as both *cis*- and all-*trans*-isomers, with certain tissues such as the prostate consisting of >80% *cis*-lycopene (5,26). Heat processing of tomato products has shown to induce the isomerization of *trans*-to *cis*-lycopene (1,30). Although

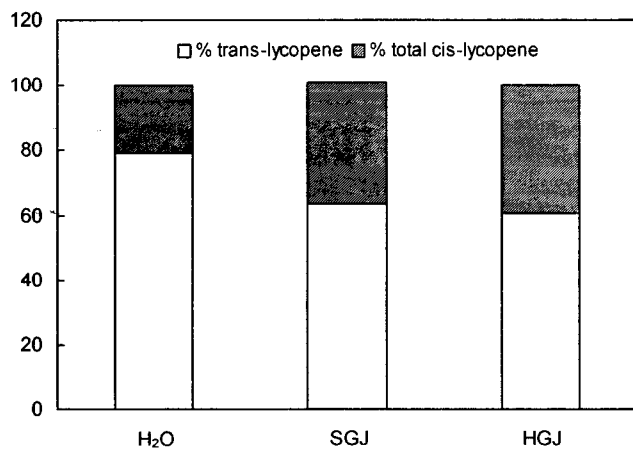


Fig. 2. The comparison of the percentage isomerization of lycopene after incubation at 37°C after 3 hours, with Water (H₂O), Simulated Gastric Juice (SGJ) and Human Gastric Juice (HGJ) (10).

all-*trans*-lycopene appears to be more stable than *cis*-forms, *cis*-lycopene is more bioavailable. This is because *cis*-lycopene is more soluble and taken up in bile acid micelles promoting absorption in the intestine (1,5,20,26, 31). The all-*trans* form of lycopene is linear and thought to be too large to be incorporated into micelles, whereas incorporation of *cis* double bonds in the lycopene structure reduces the length of the molecule therefore making incorporation into micelles easier (5). Another rationale is that the linear all-*trans* isomer aggregates in the intestine, therefore forming crystals that cannot be taken in by micelles (5). In a study by Stahl and Sies (30), it was found that levels of total lycopene increased in the serum when given tomato juice. They also observed that based on the concentration of the different isomers in the tomato juice, *cis*-isomers were absorbed at a higher rate than the all-*trans* isomers. This proves that *cis*-isomers are more bioavailable for transport and absorption than all-*trans*-lycopene. Fig. 3 shows a graphical representation of chylomicron levels of the different isomers after a single consumption of fresh tomatoes and tomato paste (21). This shows that the higher level of *cis*-lycopene in processed tomato product such as tomato paste is more bioavailable for uptake into the chylomicrons and therefore for transport to target tissues.

A hypothesis for the higher levels of *cis*-lycopene seen in serum levels after consumption of tomato juice is that *cis*-forms are metabolized to a lesser extent, or at a slower rate than *trans*-lycopene (30). However, there is no evidence to prove this statement. Therefore, with the knowledge that *cis*-lycopene is more bioavailable; tomato products that have undergone *trans-cis* isomerization are ideal in providing the beneficial health effects of lycopene.

EFFECT OF FOOD MATRIX

The release of lycopene from the food matrix is an

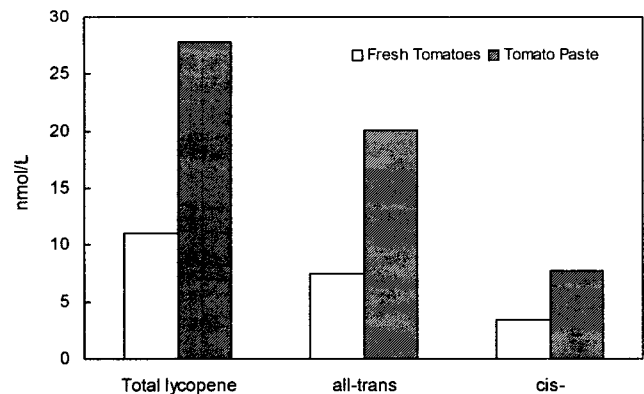


Fig. 3. Responses in chylomicrons after ingestion of fresh tomatoes and tomato paste, seen in total lycopene, all-*trans* and *cis*-lycopene (21).

important step in enhancing bioavailability. Fresh tomatoes are considered a poor bioavailable source of all-*trans* isomer lycopene. Raw tomatoes have shown to have diminutive protective effects against oxidant stress, as seen in numerous clinical trials (20,26,32). Tomato skins have been shown to have a higher level of total lycopene than the tomato pulp fraction. Most of the lycopene is attached to the insoluble fiber portion of the tomato (8,33). Bohm and Bitsch (9) discovered no significant change in the plasma levels of lycopene after the intake of fresh tomatoes compared to supplementation with a lycopene soft-gel capsule. These results have been duplicated in other similar clinical trials. Intake of tomato paste produces a higher response in the plasma than consumption of the same amount of total lycopene from fresh tomatoes (23). This is due to the higher levels of *cis*- isomers in tomato paste than fresh tomatoes. Bioavailability of tomato paste is increased by texture disruption, occurring by physical mechanical disruption and thermal processing (3,5,23,24,26). Disruption of the food matrix is considered the first step in the release of lycopene from cell walls (5,14,23). Texture disruption disperses the liposoluble portion of tomatoes by rupturing the cell walls, thereby decreasing the intactness of the cellular matrix. This in turn decreases the particle size of lycopene and increases incorporation into bile acid micelles. However, tomato products that have not undergone texture disruption become crystallized, therefore decreasing its bioavailability (3,4,21,23,26,30). van het Hof et al. (34) studied the level of bioavailability of lycopene in the plasma of subjects consuming tomatoes with different degrees of homogenization and thermal treatment. They found that both processes increased carotenoid bioavailability, although additional heat treatment to severely homogenized tomatoes did not further increase bioavailability (34). This is seen in Fig. 4, which shows the percentage of lycopene released after mild extraction. This shows that there may be a threshold effect to the degree of processing used to increase bioavailability. Lycopene in raw tomatoes is also bound to protein-complexes. Thermal processing denatures these protein complexes, therefore freeing up the lycopene for absorption (4,25,34).

The intracellular location of lycopene is a determining factor in the bioavailability of lycopene. As previously stated, in raw tomatoes most of the lycopene is bound to the insoluble fiber portion, or the pericarp (8,35). As tomatoes ripen, chromoplasts of the tomato are formed from chloroplasts. Once chromoplasts develop, carotenoids are produced and accumulated in the chromoplast (36). Tomatoes with high levels of chloroplasts, firstly have lower total lycopene levels, and secondly, are poor-

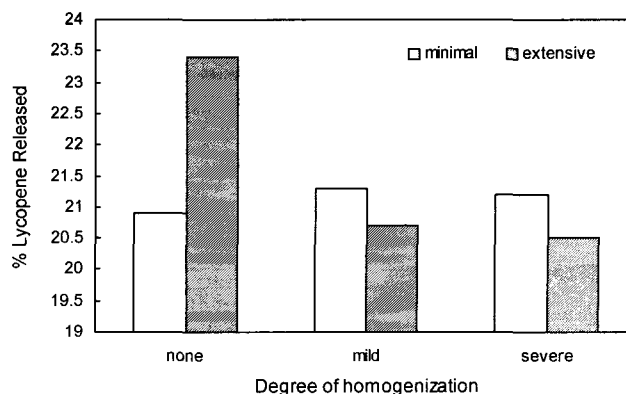


Fig. 4. *In vitro* release of lycopene from tomato products measured after mild extraction, expressed as proportion of the content measured after extensive extraction. Values are means \pm SEM $n=3$. The proportion of release was significantly different among all three degrees of homogenization for minimally additionally heated tomatoes and between severely homogenized and none or mildly homogenized for the additionally heated tomatoes. Additional heat treatment significantly enhanced the release of lycopene only for the unhomogenized and mildly homogenized tomatoes (34).

ly disrupted by the gut (23,36). Chromoplast differentiation will be an important topic when discussing the different ways to enhance lycopene bioavailability, which is discussed in a later section. Overall, the release of lycopene from its food matrix, the first step of absorption, is an important step in increasing the bioavailability of lycopene.

EFFECT OF OIL MEDIUM

Once carotenoids have been released from their food matrix, they must be incorporated into the lipid droplets and then into mixed micelles. Ingestion of fat along with lycopene is crucial, as formation of micelles is dependent on the presence of fat in the intestine (5,23,25). It was found that approximately 5 g of fat in a meal are required for optimal absorption of carotenoids (4,5,23). In fact, fat is an important factor at many stages of absorption of carotenoids. Once lycopene is released from the food matrix, it is incorporated into the lipid phase of chyme. Fat then stimulates bile secretion for the formation of micelles, and they are then packaged into chylomicrons for transport out of the mucosal cells to the general circulation for transport to the tissues (4). As previously stated, *cis*-lycopene is more bioavailable than *trans*-isomer, due to its higher solubility in the lipophilic phase in the intestine, and therefore, is incorporated into mixed micelles to a larger extent (26). Therefore, not only is the ingestion of fat with carotenoids important for bioavailability, processing tomatoes with fat will increase bioavailability prior to digestion by releasing lycopene into the lipophilic phase (4,21,30). Corn oil has been used as a vehicle for extraction of lycopene in the lipo-

philic phase in many studies. Stahl and Sies (3) found that boiling processed tomato juice for 1 hour with the presence of 1% corn oil significantly increased the bioavailability in the plasma of subjects. However, tomato juice is not usually consumed with fat, and is a poor bioavailable source of lycopene on its own, as it was shown to have no effect on plasma levels in the subjects consuming it (21).

The type of fat present during processing or ingestion also influences the level of bioavailability. Borel et al. (37) tested the response of β -carotene in meals containing long-chain fatty acids (LCFA) and medium-chain fatty acids (MCFA) in 16 healthy males. The investigators found that there was no secretion of chylomicrons with the MCFA meal, suggesting that LCFA are required for the formation of chylomicrons (37). MCFA do not form chylomicrons because they are absorbed via the portal vein (23,37). Lycopene is similarly incorporated into micelles like β -carotene 30; therefore, it is reasonable to assume that the type of fat consumed with a tomato meal will impact the bioavailability of lycopene to the target tissues. However, this must be investigated further to prove this. Lee et al. (38) conducted a study to determine whether there was a difference in plasma levels of lycopene after ingestion with olive oil and sunflower oil, oils with different fatty acid compositions. There were no significant differences in the absorption of lycopene based on the plasma levels of lycopene with both oils. However, consumption of tomato products with olive oil increased the plasma antioxidant activity, measured using a ferric-reducing ability of the plasma (FRAP) assay (38). Therefore, even though there were no significant differences in the absorption of lycopene with the consumption of the two different oils, the antioxidant capacity is an important measurement. Therefore, not only should the absorption levels of different fats with high-lycopene diets be examined, but the antioxidant potential.

Ahuja et al. (39) compared the effect of a modified diet high in monounsaturated fat to a diet rich in carbohydrates, both containing a high level of lycopene. Both diets resulted in a significant increase in total, *cis*- and *trans*-serum lycopene levels. The high fat diet showed a trend towards higher serum lycopene levels, however, these results were not significant. Therefore, in this study, the level of fat in the diet had no long term effect on serum levels of lycopene. They hypothesize that, due to increases in serum levels of short-term studies with the intake of fat with lycopene rich diets, fat may only have short-term effects of the bioavailability, however, this theory is not substantiated. Therefore, it is important to determine if there is an

optimal level of fat with carotenoid-rich diets to increase bioavailability, or if there is a saturation effect taking place.

EFFECT OF DIETARY FIBERS

The overall health of the individual impacts bioavailability, for example, poor iron, zinc, and protein status are correlated with reduced carotenoid absorption. Certain malabsorptive diseases, liver or kidney diseases or intestinal parasites also reduce carotenoid absorption (32). Fundamentally, disease states and certain dietary factors that disrupt the formation of bile acid micelles interfere with carotenoid absorption (5,14,23,31).

Fiber has important functions in maintaining gut function, by regulating the rate and site of nutrient absorption (40). Fiber slows the rate of absorption by increasing the viscosity and volume of intestinal contents. Fiber affects carotenoid absorption by partitioning bile acids and fat in the gel phase of fiber, resulting in its loss through fecal excretion (11,23,40). Studies on β -carotene showed that certain types of dietary fibers were shown to reduce absorption of carotenoids, specifically pectin (32). Chemical and physical characteristics of fiber interact with carotenoids. Riedl et al. (40) placed subjects on meal enrichments containing different types of dietary fibers plus β -carotene, lycopene, lutein, canthaxanthin, and α -tocopherol, and looked at the fibers effect on serum levels of these carotenoids and α -tocopherol. Results showed a decrease of 21.5% change in the plasma concentration of lycopene overall, showing that fiber did indeed have a significant impact in lowering the absorption of lycopene. Guar and cellulose appeared to have the biggest effect on lycopene levels, as seen in Fig. 5 (40).

Physical characteristics of fibers such as the viscosity, particle size, gel forming ability, and most importantly

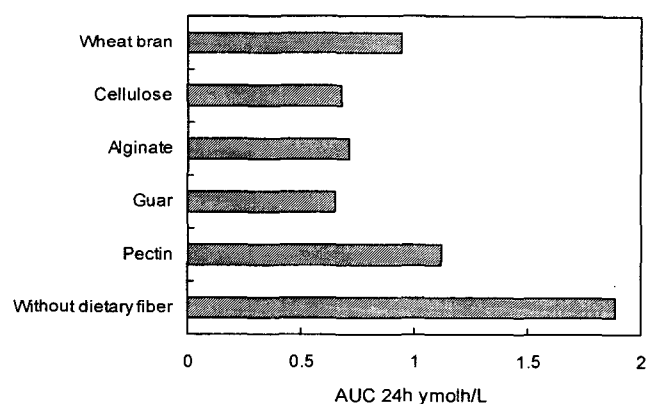


Fig. 5. Effect of different kinds of dietary fiber on the relative plasma response (AUC 24 h in % of AUC 24 h without dietary fiber) of lycopene supplementation in healthy young women (38).

the micelle-binding capacity affect carotenoid absorption and bioavailability (40). Although fiber is an important dietary component, it is important to consume low amounts with carotenoid-rich meals.

CAROTENOID INTERACTION

It is well documented that the intake of fruits and vegetables reduce the risk of chronic diseases, like cardiovascular disease and cancer. Carotenoids play a valuable role in this antioxidant effect, therefore it is important to understand the relationship they play when consumed alone and with each other. It is questioned whether carotenoids act competitively, additively, or synergistically. Intestinal absorption is a major factor in bioavailability; therefore, it is important to understand what is happening at this level. Competition for absorption occurs at various different levels of absorption, including micellar incorporation, intestinal uptake, lymphatic transport, or at a combination of these levels (23). It has been well documented that carotenoids compete for absorption into the lipid droplet, the micelle, and possibly for incorporation into the chylomicron (29,41). Tyssandier et al. (41) performed a study to test the competitive or synergistic effects of consuming various vegetable-borne carotenoids by looking at chylomicron responses in two trials. They looked at single consumption in a postprandial state and with three weeks of consumption. The subjects were fed meals high in lycopene or lutein, and both high in β -carotene. The results of the postprandial responses were drastically different from the longer-term responses. Adding spinach to tomato puree diminished chylomicron response to lycopene, as seen by using the area under the curve (AUC). Also adding lycopene to a spinach meal lowered chylomicron response to lutein. β -carotene chylomicron response was lower with the incorporation of both lycopene and lutein. This suggests that there is competition occurring between lutein, lycopene, and β -carotene for incorporation into the chylomicron. However, longer-term incorporation of meals either high in lycopene, lutein, and β -carotene showed that there was a synergistic response with all carotenoids. Results showed that plasma lycopene levels increased by 85% and 92% after consumption of a mixed meal, and by 16% after consumption of a lycopene rich meal only. This shows that there is a synergistic effect in carotenoids consumed together. The investigators suggested that other mechanisms were involved, possibly that lutein induced an antioxidant sparing effect, resulting in increased lycopene levels (41). The postprandial chylomicron responses can be seen in Fig. 6.

Other scientists shared this view as well (23,42). Stahl et al. (42) measured the antioxidant ability when con-

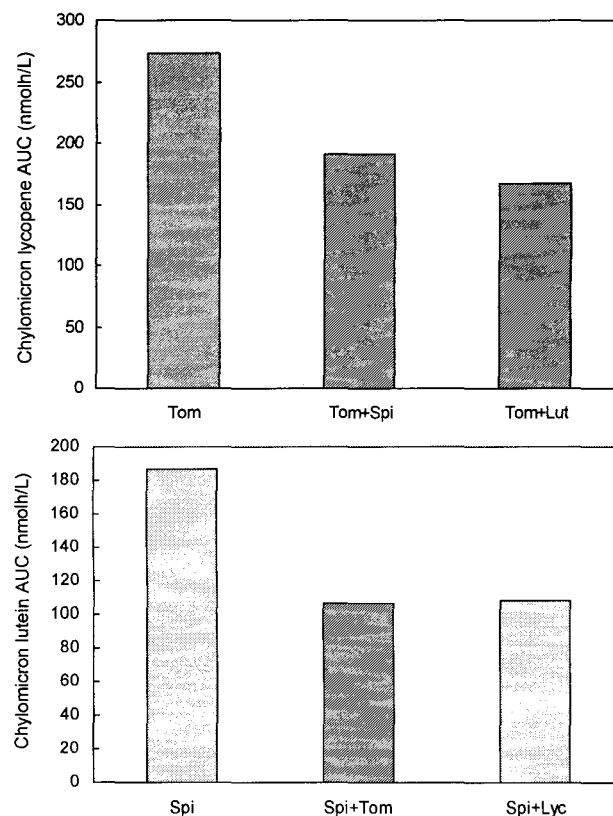


Fig. 6. AUC of the chylomicron carotenoid responses obtained after ingestion of a meal of either tomato puree (Tom), tomato puree + chopped spinach (Tom + Spi), tomato puree + lutein pills (Tom + Lut), chopped spinach (Spi), chopped spinach + lycopene pill (Spi + Lyc). Bars in the same panel with different letters are significantly different, $p < 0.05$ (ANOVA) (39).

suming carotenoid combinations and found that they had a synergistic effect. Interestingly they found by adding and omitting different carotenoids from mixtures, that lutein and lycopene appeared to be responsible for the synergistic antioxidant effect, possibly through the mechanism described above (42). Therefore, it is important to eat a diet rich in a variety of carotenoids, and other fruits and vegetables to provide the synergistic effect seen here.

ENHANCEMENT OF LYCOPENE BIOAVAILABILITY

In order to see the beneficial health effects of lycopene, it must be bioavailable to the tissues. Food processing techniques have provided a valuable tool in increasing the bioavailability of lycopene. Homogenization and heat treatment enhance carotenoid bioavailability from fresh vegetables. It does this by disrupting the cell membrane, thereby releasing lycopene from the cells. Also, heat treatment is thought to further disrupt protein-carotenoid complexes (11,21,30,34). Heat treatment is also thought to initiate *cis-trans* isomerization. Although, a study by Nguyen and Schwartz (32) found that heating alone did not initiate lycopene isomerization, but the

presence of lipids combined with heating improved lycopene bioavailability. However, a study by Boileau et al. (5) found that there was a moderate increase in *cis*-isomerization with heat treatment. Therefore, there may be other factors affecting the outcome. The presence of lipids, either ingested with the lycopene-rich meal or added during food processing, increases bioavailable lycopene. Stahl and Sies (30) found that boiling processed tomato juice in the presence of 1% corn oil significantly increased the bioavailability of lycopene, as measured in the human serum. It should be explored whether certain oils enhance lycopene to a greater degree than other oils. Presently, most studies have used corn oil to test this. Also, the role that stomach acid plays in enhancing bioavailability is relatively unknown. The acidity of the stomach is thought to initiate *cis-trans* isomerization of lycopene; therefore, it may be of importance to test the effect of the addition of cooking acids in processing, to test if isomerization occurs. Rich et al. (43) conducted a study that tested the effect of both oil and acid in relation to the transfer of carotene to the lipid phase of absorption. They found that a lower pH, or higher acidity increased the amount of carotene transferred into the oil. Also a low pH enhanced the transfer of crystals from the chromoplast into the oil phase, showing that partitioning is pH-dependent. The addition of a low acid in oil and carotenoid mixtures may alter the electric potential of the mixture interface, therefore enhancing incorporation, also by bringing the crystals and oil droplets closer together therefore enhancing carotenoid passage through the oil-water interface to dissolve in the oil (43). It would be beneficial to test whether there is a synergistic or additive effect with the addition of both lipids and acid during the processing of carotenoid-rich products.

Agricultural practices have been trying to discover new ways of increasing the levels of total lycopene in raw tomatoes by genetic crosses or genetic manipulations in order to increase the amount of lycopene in a typical diet (1). There is presently Genetically Modified high lycopene tomatoes on the market. Ishida et al. (35) performed a study to test the effects of the addition of 2-(4-chlorophenylthio)triethylamine (CPTA) *in vitro* in the fruit and calyces of tomatoes. CPTA increased lycopene levels in the fruits and calyces of tomatoes. CPTA is thought to enhance chromoplast differentiation and increase synthesis of proteins and enzymes involved in the lycopene synthesis pathway. However, CPTA is attributed to the blocking of lycopene cyclization to β -carotene (35). By increasing the levels of lycopene in the raw tomato, it is possible to increase the levels of bioavailable lycopene even further with processing.

However, this needs to be examined further in order to determine this.

HEALTH BENEFITS OF LYCOPENE

Possibly the most important health effect of lycopene is its ability to deactivate singlet oxygen species and act as free radical scavengers. Free radicals are one of the main culprits in the etiology of many chronic diseases, such as cardiovascular disease and cancers. Disease prevention is becoming an important concern for medical researchers and the general public alike. Tomatoes contain a number of other very important nutrients, such as folate, potassium, and vitamin C (44). The Mediterranean diet is widely known to contain high lycopene intake from tomato products. The beneficial effects seen in the Mediterranean diet was first suggested on the basis of the low mortality from cardiovascular diseases and cancers, like intestinal, pancreas, breast and prostate cancers, in these countries (17). The mechanism of action in the prevention of cardiovascular disease involves lowering the formation of oxidized LDL. Oxidized LDL form inflammatory products such as foam cells, which is a precursor in the formation of arterial plaques (18,24). The formation of arterial plaques increases the risk of coronary heart disease. The preferential incorporation of ingested lycopene into LDL, with 75% of lycopene and β -carotene associated with LDL, provides great protection against oxidative damage (45).

The onset of many cancers is due to the oxidation of DNA molecules resulting in the formation of mutagenic and carcinogenic compounds. Lycopene reduces DNA oxidative damage and blocks the conversion of food mutagens, mainly heterocyclic amines found in fried or cooked foods, through its free radical and oxygen quenching ability, thereby lowering the risk of many cancers (18,24). Interestingly, plasma lycopene levels were not affected by cigarette smoking like β -carotene; furthermore, the formation of lung tumors in mice given lycopene was significantly lower (18). This is because lycopene is a good inhibitor of cell proliferation, thereby decreasing cancerous cell formation. The incorporation of lycopene-rich tomato products, with other carotenoid fruits and vegetables, may play a role in the prevention of chronic diseases, thereby increasing the quality of life of individuals and decreasing health care costs associated with these diseases.

CONCLUSION

Carotenoids are an important part of a healthy diet and help in the prevention of cardiovascular disease and many cancers by decreasing oxidative damage. Lycopene is considered the most potent free radical scavenger and

singlet oxygen quencher of all of the nearly 600 carotenoids. But in order to be incorporated into chylomicron LDL particles and reach the tissues to exert its protection, it must be in a bioavailable form. There are many dietary interactions that influence the bioavailability of lycopene, both negatively and positively. These findings are being incorporated into food processing and agricultural practices in order to maximize the amount of lycopene intake in the usual diet. Enhancement of total lycopene and lycopene bioavailability is a growing concern in food science practices. Lycopene is being added to products in the form of nutraceuticals, by adding lycopene concentrate to multivitamins, or in functional food products. Many of the processed tomato products are considered functional food products because they already provide an enhanced lycopene product to consumers. However, products could be made with the pure compound added, as it provides a higher order of bioavailability than when naturally present in foods.

There still needs to be additional studies conducted on the effects of processing tomato products with different types of fat and acid, in order to initiate *cis-trans* isomerization and thereby increasing bioavailability. There are currently no studies that have looked at the effects of processing with different kinds of oils on the market to see if there is a difference in the enhancement potential. It is already known that medium chain fatty acids do not increase bioavailability, as they do not stimulate micelle formation, however long chain fatty acids have been shown to. Therefore it would be interesting to see if there was a difference in enhancement using several different LCFA during the processing of tomatoes, and then analyze the change in the different isomer levels. Therefore, more research is needed in order to fully understand the many interactions that occur in order to increase lycopene bioavailability.

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REFERENCES

1. Bramley P. 2000. Is lycopene beneficial to human health? *Phytochemistry* 54: 233-236.
2. Shi J, Le Maguer M. 2000. Lycopene in tomatoes: Chemical and physical properties affected by food processing. *Crit Rev Food Sci Nutr* 40: 1-42.
3. Stahl W, Sies H. 1996. Lycopene: A biologically important carotenoid for humans? *Arch Biochem Biophys* 336: 1-9.
4. Williams A, Boileau T, Erdman Jr. 1998. Factors influencing the uptake and absorption of carotenoids. *Proc Soc Exp Biol Med Jun* 218: 106-108.
5. Boileau TW, Boileau AC, Erdman JW Jr. 2002. Bioavailability of all-trans and cis-isomers of lycopene. *Exp Biol Med* (Maywood). 227: 914-919.
6. Van Breemen RB, Xu X, Viana MA, Chen L, Stacewicz-Sapuntzakis M, Duncan C, Bowen P, Sharifi R. 2002. Liquid chromatography-mass spectrometry of cis- and all-trans-lycopene in human serum and prostate tissue after dietary supplementation with tomatoe sauce. *J Agr Food Chem* 50: 2214-2219.
7. Ishida B, Ma J, Chan B. 2001. A simple, rapid method for HPLC analysis of lycopene isomers. *Phytochem Anal* 12: 194-198.
8. Sharma S, Maguer M. 1996. Lycopene in tomatoes and tomato pulp fractions. *Ital J Food Sci* 2: 107-113.
9. 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. *Eur J Nutr* 38: 118-125.
10. Re R, Fraser PD, Long M, Brameley PM, Rice-Evans C. 2001. Isomerization of lycopene in the gastric milieu. *Biochem Biophys Res Commun* 281: 576-581.
11. Castenmiller J, West C, Linssen J, van het Hof K, Voragen A. 1999. The food matrix of spinach is a limiting factor in determining the bioavailability of beta-carotene and to a lesser extent of lutein in humans. *J Nutr Feb* 129: 349-55.
12. Olson JA. 1994. Absorption, transport, and metabolism of carotenoids in humans. *Pure & Appl Chem* 66: 1011-1016.
13. Clinton S, Giovannucci E. 1998. Diet, nutrition, and prostate cancer. *Annu Rev Nutr* 18: 413-440.
14. Giovannucci E, Clinton S. 1998. Tomatoes, lycopene, and prostate cancer. *Proc Soc Exp Biol Med* 218: 129-139.
15. Sies H, Stalh W. 1998. Lycopene: Antioxidant and biological effects and its bioavailability in the human. *Proc Soc Exp Biol Med* 218: 121-124.
16. Sundquist A, Hanusch M, Stalh W, Sies H. 1993. Cis/trans isomerization of carotenoids by the triplet carbonyl source 3-hydroxymethyl-3,4,4-trimethyl-1,2-dioxetane. *Photochemistry and Photobiology* 57: 785-791.
17. Vecchia C. 1998. Mediterranean epidemiological evidence on tomatoes and the prevention of digestive-tract cancers. *Proc Soc Exp Biol Med* 218: 125-128.
18. Weisburger J. 1998. Evaluation of the evidence on the role of tomatoe products in disease prevention. *Proc Soc Exp Biol Med* 218: 140-143.
19. Zhao Z, Khachik F, Richie J Jr, Cohen L. 1998. Lycopene uptake and tissue disposition in male and female rats. *Proc Soc Exp Biol Med* 218: 109-114.
20. Krinsky N. 1998. Overview of lycopene, carotenoids and disease prevention. *Proc Soc Exp Biol Med* 218: 95-100.
21. Gartner C, Stahl W, Sies H. 1997. Lycopene is more bioavailable from tomato paste than from fresh tomatoes. *Am J Clin Nutr* 66: 116-122.
22. Krinsky N. 1994. The biological properties of carotenoids. *Pure & Appl Chem* 66: 1003-1010.
23. van het Hof K, West C, Westrate J, Hautvast J. 2000. Dietary Factors that affect the bioavailability of carotenoids. *J Nutr* 130: 503-506.
24. Agarwal A, Shen H, Agarwal S, Rao AV. 2001. Lycopene content of tomato products: Its stability, bioavailability and *in vivo* antioxidant properties. *J Med Food* 4: 9-15.
25. Johnson E. 1998. Human studies on bioavailability and plasma response of lycopene. *Proc Soc Exp Biol Med* 218: 115-120.
26. Richelle M, Bortlik K, Liardet S, Hager C, Lambelet P, Baur M, Applegate L, Offord E. 2002. A Food-based for-

- mulation provides lycopene with the same bioavailability to humans as that from tomato paste. *J Nutr* 132: 404-408.
27. Hadley C, Clinton S, Schwartz S. 2003. The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidative damage. *J Nutr* 133: 727-732.
 28. Paetau I, Rao D, Wiley E, Brown E, Clevidence B. 1999. Carotenoids in human buccal mucosa cells after 4 wk of supplementation with tomato juice of lycopene supplements. *Am J Clin Nutr* 70: 490-494.
 29. Tyssandier B, Reboul E, Dumas JF, Bouteloup-Demange C, Armand M, Marcand J, Sallas M, Borel P. 2003. Processing of vegetable-borne carotenoids in the human stomach and duodenum. *Am J Physiol Gastrointest Liver Physiol* 284: G913-923.
 30. Stahl W, Sies H. 1992. Uptake of lycopene and its geometrical isomers is greater from heat-processed than from unprocessed tomato juice in humans. *J Nutr* 122: 2161-2166.
 31. Wu K, Schwartz SJ, Platz EA, Clinton SK, Erdman JW Jr, Ferruzzi MG, Willett WC, Giovannucci EL. 2003. Variations in plasma lycopene and specific isomers over time in a cohort of US men. *J Nutr* 133: 1930-1936.
 32. Nguyen M, Schwartz S. 1998. Lycopene stability during food processing. *Proc Soc Exp Biol Med* 218: 101-105.
 33. Sharma S, Maguer M. 1996. Kinetics of lycopene degradation in tomato pulp solids under different processing and storage conditions. *Food Research International* 29: 309-315.
 34. van het Hof K, de Boer B, Tijburg LBM, Lucius B, Zijp I, West C, Hautvast J, Weststrate J. 2000. Carotenoid bioavailability in humans from tomatoes processed in different ways determined from the carotenoid response in the triglyceride-rich lipoprotein fraction of plasma after a single consumption and in plasma after four days of consumption. *J Nutr* 130: 1189-1196.
 35. Ishida B, Mahoney N, Ling L. 1888. Increased lycopene and flavor volatile production in tomato calyces and fruit cultered *in vitro* and the effect of 2-(4-chlorophenylthio) triethylamine. *J Agric Food Chem* 46: 4577-4582.
 36. Cheung AY, McNellis T, Piekos B. 1993. Maintenance of chloroplast components during chromoplast differentiation in the tomato mutant green flesh. *Plant Physiol* 101: 1223-1229.
 37. Borel P, Tyssandier V, Mekki N, Grolier P, Rochette Y, Alexandre-Gouabau M, Lairon D, Azais-Braesco V. 1998. Chylomicron β -carotene and retinyl palmitate responses are dramatically diminished when men ingest β -carotene with medium-chain rather than long-chain triglycerides. *J Nutr* 128: 1361-1367.
 38. Lee A, Thurman D, Chopra M. 2000. Consumption of tomato products with olive oil but not sunflower oil increases the antioxidant activity of plasma. *Free Radical Biol & Med* 29: 1051-1055.
 39. Ahuja KDK, Ashton EL, Ball MJ. 2003. Effects of a high monounsaturated fat, tomato-rich diet on serum levels of lycopene. *Eur J Clin Nutr* 57: 832-841.
 40. Riedl J, Linseisen J, Hoffmann J, Wolfram G. 1999. Some dietary fibers reduce the absorption of carotenoids in women. *J Nutr* 129: 2170-2176.
 41. Tyssandier V, Cardinault N, Caris-Veyrat C, Amiot MJ, Grolier P, Bouteloup C, Azais-Braesco V, Borel P. 2002. Vegetable-borne lutein, lycopene, and beta-carotene compete for incorporation into chylomicrons, with no adverse effect on the medium-term (3-wk) plasma status of carotenoids in humans. *Am J Clin Nutr* 75: 526-534.
 42. Stahl W, Junghans A, de Boer B, Driomina ES, Briviba K, Sies H. 1998. Carotenoid mixtures protect multilamellar liposomes against oxidative damage: synergistic effects of lycopene and lutein. *FEBS Lett* 427: 305-308.
 43. Rich G, Fillery-Travis A, Parker M. 1998. Low pH enhances the transfer of carotene from carrot juice to olive oil. *Lipids* 33: 985-992.
 44. Beecher GR. 1998. Nutrient content of tomatoes and tomato products. *Proc Soc Exp Biol Med* 218: 98-100.
 45. Parker R. 1989. Carotenoids in human blood and tissues. *J Nutr* 118: 101-104.

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