Chapter

Potential of Carotenoids from Fresh Tomatoes and Their Availability in Processed Tomato-Based Products

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Abstract

The high consumption of tomatoes worldwide has made them an essential source of health-promoting carotenoids that prevent a variety of chronic degenerative diseases, such as diabetes, high blood pressure, and cardiovascular disease. Tomatoes are available year-round, consumed fresh, and used as a raw material for the production of many processed products, such as juices, pastes, and purees. A plethora of carotenoids has been characterized in tomatoes. Most of the relevant carotenoids in the human bloodstream are supplied by fresh and processed tomatoes. Lycopene is the predominant carotenoid in tomato and tomato-based food products. Other carotenoids such as α-, β-, γ- and ξ-carotene, phytoene, phytofluene, neurosporene, and lutein are present in tomatoes and related products. There is a growing body of evidence that these bioactive compounds possess beneficial properties, namely anti-carcinogenic, cardioprotective, and hepatoprotective effects among other health benefits, due to their antioxidant, anti-mutagenic, anti-proliferative, anti-inflammatory, and anti-atherogenic properties. This chapter analyzes the carotenoid composition of tomatoes and their based products as major contributors to the chronic disease-preventive properties.

Keywords: tomato, carotenoids, health, antioxidant, chronic diseases

1. Introduction

Tomato (*Solanum lycopersicum* L.) belongs to the Solanaceae family and is one of the most important and versatile crops in the world. Wild tomato is originated in western South America along the coast and the high Andes from central Ecuador, through Peru, to northern Chile, and in the Galapagos Islands [1–5]. The period and center of domestication of tomatoes are still unclear, but it is believed that the region of domestication was Central America [1–3]. Nowadays, with several selected cultivars adapted to different edaphoclimatic conditions and final food products, tomato is cultivated worldwide and marketed either as fresh or as processing tomato [4]. The global tomato production reached 186,821,216 tons in 2020. According to FAOSTAT, the world's top three tomato producers in 2020 were China, India, and Turkey [6].

Tomato consumption is dominant in China, India, North Africa, the Middle East, the US, and Brazil [5]. They are consumed either fresh in salads or cooked in sauces, soup, and various dishes. In addition, they can be processed into paste, purées, juices, and ketchup. Canned and dried tomatoes are economically important processed products, they contain abundant minerals, essential amino acids, sugars, and dietary fibers [4] as well as many health-promoting compounds including vitamins, carotenoids, and phenolic compounds [5]. Although these bioactive constituents could be obtained through intake of dietary supplements, scientific evidence suggests that direct intake from their natural matrix is much more effective regarding health benefits [7].

Carotenoids are well-known bioactive compounds involved in preventing the development of diseases such as diabetes, gastrointestinal and cardiovascular diseases (CVDs), for example, by reducing the amount of oxidized low-density lipoproteins (LDLs). They are also known to reduce the risk of developing degenerative diseases such as blindness, xerophthalmia, and degeneration of muscles. In addition, carotenoids possess anticancer properties in health conditions, such as stomach, lung, and prostate cancers [3], being this disease-preventing action attributed to their antioxidant components. Lycopene and β-carotene are carotenoids with particularly strong antioxidant activities, based on their abilities to quench singlet oxygen and trap peroxyl radicals [8]. In this chapter, the potential of tomato carotenoids in chronic disease prevention is discussed. The role and types of carotenoids are presented, after which the composition and distribution of carotenoids in tomato and tomato-based products are documented. The factors influencing the bioavailability of tomato carotenoids are explained. Finally, the action of carotenoids in the risk reduction of non-communicable diseases is detailed.

2. Carotenoids: definition, classification, and food sources

Carotenoids represent a large family of non-water-soluble pigments that range from yellow to red and are predominantly found in fruits and vegetables [9, 10]. Generally, carotenoids are a class of isoprenoid molecules that are commonly referred to as pigments due to their characteristic yellow to red color. This physical property is due to a polyene chain containing 3–13 conjugated double bonds that act as a chromophore. All photosynthetic organisms (such as plants and algae) and some non-photosynthetic bacteria and fungi synthesize carotenoids that are tetraterpenes (terpenes consisting of eight isoprene units, $C_{40}H_{64}$) derived from phytoene, a 40-carbon isoprenoid [11, 12]. Some carotenoids called higher carotenoids are made up of a 45- or 50-carbon skeleton, while those having carbon skeletons with fewer than 40 carbons are called apocarotenoids [13]. Carotenoids can be synthesized de novo by flora and microbes, and do not occur naturally in mammals with minor exceptions [14]. Therefore, carotenoids found in animal tissues are either directly obtained from their diets or partially modified during metabolic reactions [15, 16]. Carotenoids are essential compounds in all photosynthetic species, such as algae, cyanobacteria, and plants, and are involved in basic physiological processes, such as photoprotection and photosynthesis. They serve numerous important functions, such as light-harvesting, photoprotection during photosynthesis, and photo-oxidative damage prevention, and also accumulate in non-photosynthetic organs of plants, such as fruits, pericarps, seeds, roots, and flowers. They provide color to flowers and fruits which is useful in pollination and seed dispersal through pollination vector attraction. They also serve as precursors for the biosynthesis of the phytohormone, abscisic acid (ABA) in non-photosynthetic organs [12, 13, 16].

2.1 Classification of carotenoids

Carotenoids can broadly be classified into two subgroups according to their chemical structure—(1) carotenes (hydrocarbon carotenoids), which are made up of carbon and hydrogen. Examples of carotenes include α-carotene, β-carotene, β, ψ-carotene (γ-carotene), and lycopene; (2) oxycarotenoids or xanthophylls (oxygenated carotenoids), which are derivatives of the hydrocarbons (carotenes) and are constituted by carbon, hydrogen, and oxygen atom in the form of hydroxy, epoxy, or oxy groups. Examples of xanthophylls include β-cryptoxanthin, lutein, zeaxanthin, astaxanthin, fucoxanthin, and peridinin [13, 14, 16, 17, 22]. Moreover, carotenoids are divided into primary or secondary. Primary carotenoids are compounds required by plants in photosynthesis (β-carotene, violaxanthin, and neoxanthin), whereas secondary carotenoids are localized in non-photosynthetic organs of plants, such as fruits and flowers (α-carotene, β-cryptoxanthin, zeaxanthin, antheraxanthin, capsanthin, and capsorubin) [14].

2.2 Carotenoids in foods

More than 700 naturally occurring carotenoids have been identified, and new carotenoids are continuously identified [17]. The nutritionally important carotenoids

Carotenoid	Food sources	Health properties
β-Carotene	Carrot, sweet potato, mango [18], pumpkin, kale, apricots, pepper, tomato paste [18], cassava [23]	Protection against oxidative stress due to the inactivation of reactive oxygen species (ROS) [20] Anticancer properties [20] Risk reduction of CVDs [24] Protects against macular degeneration and reduces aging [25]
α-Carotene	Spinach, cantaloupe [21] Tomato [28, 29]	Antioxidant and anticarcinogenic agent [21, 24]
Lycopene	Tomato and processed products, red carrot, red bell pepper, watermelon, papaya [18]	Decreased risk of prostate cancer [18] Strong antioxidant effect due to the inactivation of ROS and the quenching of free radicals [20] Anticancer properties [24] Risk reduction of CVDs [24] Reduce the risk of macular degeneration [25]
β-Cryptoxanthin	Oranges, papaya, peaches, tangerines, maize (yellow/orange) [26] mangoes [21], tomato [28, 29]	Antioxidants and anticancer properties [21] Antimutagenic and immunomodulatory activities [24] Protective against lung cancer and improved lung function [26]
Lutein	Tomato, goji berry, romaine lettuce, zucchini, kiwifruit, garden peas, olive [18], parsley, broccoli, avocado, Brussels sprouts, beans [21], corn [23]	Protective action against ocular diseases such as macular degeneration and cataract [23] Antioxidant agents [24] improves visual acuity, scavenges harmful ROS [25]
Zeaxanthin	Same as lutein Mandarins, peaches, oranges [21]	Protects against macular degeneration and cataract [23] Antioxidant properties [24] improves visual acuity, scavenges harmful ROS [25]

Table 1.
Major dietary carotenoids and their health properties.

in human foods include the carotenes; β-carotene, α-carotene, and lycopene and the xanthophylls; β-cryptoxanthin, lutein, and zeaxanthin. These nutritionally important carotenoids are of major interest because they are detectable in the human plasma and can further be classified into provitamin A and non-provitamin A carotenoids. Provitamin A carotenoids are β-carotene, α-carotene, and β-cryptoxanthin, whereas non-provitamin A carotenoids are lutein, zeaxanthin, and lycopene [18]. Provitamin-A carotenoids are a major source of vitamin A, when ingested by human beings, they are converted into vitamin A, which has several important functions including vision, immune response, bone mineralization, reproduction, cell differentiation, and growth [19].

β-Carotene is the most widely distributed carotenoid in the human diet. α-Carotene is usually detected in similar foodstuff as β-carotene but in lower quantities. **Table 1** summarizes the main carotenoids in foodstuff and their effects on human health.

3. Carotenoids in tomato and processed products

3.1 Carotenoids in fresh tomato

Carotenoids are highly abundant in tomatoes [27]. Over 20 carotenoids have been previously characterized in tomato and tomato-based products, this includes lycopene, α-carotene, β-carotene, γ-carotene, ξ-carotene, ζ-carotene, phytoene, phytofluene, cyclolycopene, neurosporene, lutein, violaxanthin, neoxanthin, zeaxanthin, α-cryptoxanthin, and β-cryptoxanthin [28, 29]. The carotenoid content in tomato fruits is unevenly distributed and its composition is highly dependent on the cultivar (genotype), degree of maturation, climatic conditions, environmental factors, and cultural practices [7, 20, 30]. The maximum quantity of total carotenoids and lycopene is found in the outer pericarp, while the locules have a high proportion of carotene compounds [31].

Carotenoids are synthesized in the leaves, flowers, and fruits of tomato plants. Lutein is found in high quantities in the leaves where it functions as a photoreceptor

Tomato type	Analytical method	Carotenoid concentrations [mg/100 g fresh weight (FW)]	Reference
Cherry tomato	High-performance liquid chromatography with diode-array detection (HPLC-DAD)	Phytoene (0.43–2.01) Phytofluene (0.12–0.8) β-Carotene (1.16–4.15) Lycopene (0.17–9.66)	[32]
Industrial (processing) tomato	HPLC-DAD and HPLC	Phytoene (5.57–10.75) Phytofluene (1.89–3.55) ζ-Carotene (3.01–7.07) Neurosporene (0.8–1.74) β-Carotene (0.23–0.45) Lycopene (3.51–11.61) Lutein (0.076–0.429)	[32, 33]
Tomato for salad	HPLC	Lutein (0.077–0.338) Lycopene (5.18–8.47) β-Carotene (0.29–0.62)	[33]

Table 2.
Mean carotenoid composition of ripe fruits of different types of tomato.

during photosynthesis. The xanthophylls, violaxanthin, and neoxanthin are abundant in flowers and are responsible for their characteristic yellow coloration. The ripe fruits of *Lycopersicum esculentum* owe their intense red color to the lycopene, the main carotenoid at this maturity stage [7]. The most widely available carotenoids in ripe tomato fruits are lycopene (≈90%), β-carotene (≈5–10%), and lutein (<1%). Lycopene and β-carotene are mainly responsible for the characteristic color of ripe tomatoes [30]. These carotenoids are important components for the determination of quality characteristics of fresh tomatoes in routine analyses [16, 30]. **Table 2** shows the carotenoid profile of cultivars from different types of tomatoes.

There is a diverse carotenoid profile within tomato cultivars. This is particularly true for traditional varieties constituting a wide source of genetic variation [25]. Tomatoes are abundant sources of lycopene, with average concentrations ranging from 8 to 40 μg/100 g of FW. This represents about 80% of the total dietary intake of this carotenoid [34]. Lycopene is a polyunsaturated compound containing 13 double bonds that can exist in *trans*- and *cis* configurations. In fresh tomatoes, lycopene is principally found in *trans*-conformation [35]. Lycopene is synthesized massively during tomato ripening. Consequently, the highest content of lycopene is observed in ripe tomato fruits [7, 27, 29]. Open field-cultivated tomatoes were reported to have a higher lycopene content (ranging from 5.2 to 23.6 mg/100 g FW) than greenhouse-cultivated tomatoes (0.1 to 10.8 mg/100 g FW) [35].

The β-carotene content in tomatoes is approximately one-tenth of the lycopene content [31]. β-Carotene is equally an essential carotenoid identified in tomatoes, of special interest mainly due to its pro-vitamin A activity [33]. In commercial cherry tomatoes, β-carotene quantity reached 1.26 mg/100 g FW (**Table 2**). The uniqueness of β-carotene is that it is the most powerful precursor to vitamin A (comprised of retinol, retinal, and retinoic acid, which are classified as retinoids). Vitamin A activity can be measured as retinol equivalents (RE) or retinol activity equivalents (RAE). Current assumptions regarding the RAE or RE of the three major provitamin A dietary carotenoids based on their bioavailability from foods, consider β-carotene as a prominent contributor to the vitamin A intake with potential for conversion to retinol, which is twice that of α-carotene and β-cryptoxanthin [36]. The central oxidative cleavage of β-carotene in the intestine catalyzed by β-carotene 15,15′-monooxygenase allows for its conversion to two molecules of vitamin A, compared to one molecule from another provitamin A carotenoids [37]. Lesser amounts of lutein are present in tomatoes, with concentrations up to 338 μg/100 g FW (**Table 2**). Raw tomato purchased from the supermarket was reported to have lutein concentrations up to 32 μg/100 g FW, against a lutein content up to 800 μg/100 g FW reported in a cherry tomato variety [35]. Other carotenoids identified in tomatoes are the colorless hydrocarbon carotenoids (carotenes), phytoene, and phytofluene, precursors of colorful carotenoids such as lycopene and β-carotene [25].

3.2 Carotenoids in processed tomato products

Although tomatoes are consumed fresh, over 80% of tomato intake is in the form of processed products, such as tomato pulp, ketchup, juice, and sauce [38]. During food processing, the naturally occurring carotenoid composition of products is altered. Reactions induced by heat, acids, light, or oxygen exposure occur as a consequence of the processing steps [39]. Thermal treatment is responsible for an increased level of total carotenoid content and antioxidant capacity by 30% and 15%, respectively. Tomato processing may activate the enzymes ε- and β-carotene cyclase,

Tomato Product	Analytical method	Carotenoid concentrations (mg/100 g FW)	Reference
Ketchup	HPLC	Lycopene (18.80–100.87) β-Carotene (0.46–10)	[41]
Canned cherry tomatoes	HPLC	Lycopene (11.42–11.78) β-Carotene (0.74–0.76) Lutein (0.14–0.16)	[42]
Tomato Purée	HPLC	Lycopene (53.36–128.60) β-Carotene (0.40–2.80)	[41]

Table 3.
Concentration of carotenoids in processed tomato products.

involved in the synthesis of β- and α-carotene. Consequently, stimulating the production of α- and β-carotene [40]. The concentrations of carotenoids in different tomato products are depicted in **Table 3**.

During tomato processing, an increase in carotenoid content on a fresh weight basis is observed as a result of water loss [41]. This may also be ascribed to the technological treatments of pasteurization and homogenization which can improve the extractability of pigments from the fruit matrix. For canned tomato products, the carotenoid increase can be explained by the use of tomato juice derived from high ripening stage tomatoes with very high lycopene content [42]. Increased content of the major tomato carotenoids, lycopene, and β-carotene was reported after processing at 45°C (drying) and 95°C (thermal treatment of tomato juice) [43]. Similarly, an increase in lycopene content in tomatoes exposed to drying at 42°C was previously demonstrated. This occurs due to the release of lycopene bound from the tissues [44]. A decrease in the lycopene content of dried tomatoes treated at 55–110°C was found [45–47]. On a dry weight basis, there is an increase or decrease of the lycopene content depending on the origin of the tomato variety, while the β-carotene content reduces or remains relatively constant [41]. Nevertheless, in certain instances, processing causes little or no change in the content and activity of naturally occurring bioactive compounds [48].

4. Bioavailability of tomato carotenoids

Only 25 carotenoids are present in the human bloodstream, out of approximately 40 carotenoids present in foods normally included in the human diet and most of these carotenoids found in human blood are present just in fresh tomato and related products [43]. This is due to the selective intake of carotenoids in the gastrointestinal tract and the food matrix surrounding them [16, 43]. Carotenoids present in the human serum tend to be associated with specific body tissues. For example, lycopene is concentrated in the prostate, β-carotene is concentrated in the corpus luteum, and lutein and zeaxanthin are concentrated in the neural retina and brain neocortex. These carotenoids can retard the development of disease at these locations based on reducing inflammatory and oxidative stress [49]. For carotenoid intake, the food matrix made up of fiber or protein must first be broken down by mastication, gastric acid, pancreatic enzymes, and bile acids to ensure the release of these nutrients [16]. Carotenoid release from the tomato matrix and its subsequent incorporation in the oil and micellar phase are crucial steps in rendering these compounds bioavailable during digestion [19]. There is a great variation in the bioaccessibility and bioavailability of different dietary carotenoids between the type of food consumed (whether it is chopped or pureed, raw or cooked, and whether or not fat is consumed simultaneously), and for a given carotenoid in different foods [36, 50]. Bioaccessibility is defined as the fraction of carotenoid released during digestion from the food matrix to mixed micelles and thus, made accessible for absorption in the gut following digestion [51], whereas bioavailability of carotenoids is the amount of these micronutrients that are absorbed by the intestinal absorptive cell, transported in the bloodstream and/or deposited in target tissues where it can exert its biological function [52].

4.1 Processing effects on tomato carotenoid bioavailability

The bioavailability of carotenoids is higher from processed foods than their raw or less processed counterparts [52]. In general, the relative bioavailability of carotenoids has been estimated to vary from less than 10% in raw, uncooked vegetables to 50% in oils or commercial preparations [50]. Processing techniques such as grinding, marinating, fermentation, freezing, and moderate heating improve the release and absorption of carotenoids. This is explained by the release of these nutrients from the food matrix as a result of the disruption of plant tissues and the transfer of carotenoids to the lipid carrier. It is believed that since carotenoids in plant tissues occur in the form of complexes with proteins, mild thermal processes allow them to break down these connections and destroy cellulose structures in plant cells, thus contributing to an increase in the absorption of these compounds [53]. The bioavailability of β-carotene is improved as a result of gentle heating or enzymatic disruption of the vegetable cell wall structure during processing [48]. Lycopene bioavailability is higher in thermally processed tomato products, such as paste, puree, ketchup, juice, soup, and sauce, than in fresh tomatoes [33, 35, 54]. This fact could be attributed to the lower availability of lycopene from the raw tomatoes where it is probably bound in the surrounding food matrix [55]. The incorporation of oil in tomato sauce has been reported to enhance the accessibility and extractability of carotenoid compounds in tomatoes. A constant quantity of fat and other ingredients significantly increases the bioavailable lycopene in tomato paste compared to fresh tomatoes [40]. Previous research demonstrated that a combination of homogenization and heat treatment improves the bioavailability of carotenoids from fruits and vegetables. Studies on the effect of heat treatment and homogenization on the carotenoid bioavailability of industrially heat-treated peeled and canned tomatoes have shown that blood plasma lycopene responses increased with increasing degree of homogenization and additional heat treatment, while homogenization enhanced the plasma response of β-carotene only if the tomatoes were not subjected to additional heat treatment [56]. Moreover, high-pressure homogenization has a greater impact on the bioavailability of carotenoids compared to homogenization under normal pressure, since it disrupts extra cell membranes [42].

4.2 Effect of isomerization on bioavailability

The physical state of carotenoids has been proven to significantly impact their bioaccessibility and bioavailability and consequently their health-promoting properties [39]. Carotenoids exist in a variety of geometric isomers and predominantly occur in their all-trans conformation in fresh tomatoes. For instance, trans-lycopene accounts for approximately 95% of the lycopene present in raw tomatoes [48]. Food processing may induce the formation of cis isomers possessing different biological properties. Trans-to-cis isomerization can also be initiated during storage [55]. Trans-isomers are thermodynamically more stable, whereas cis are more polar, more soluble in oil and hydrocarbon solvents, and are less prone to crystallization than their all-trans counterparts [38, 55]. More than 50% of the carotenoids identified in the human body are in the cis configuration, suggesting that this is the most bioavailable form [40]. Several reports have demonstrated that the cis isomers of lycopene are more bioavailable and play a more important biological function than all-trans lycopene properties [57, 58] because of being more soluble and easily absorbed from the intestinal lumen than the trans-lycopene [59]. Therefore, lycopene from processed tomato products is generally more bioavailable than the one from the unprocessed counterparts. Nevertheless, inadequate processing and storage conditions can cause isomerization during the byproducts' formation, diminishing the absorption of carotenoids and making the product less desirable to the consumer [19]. On the other hand, cellular studies reported that cis isomers of β-carotene are not easily absorbed by intestinal enterocytes. High quantities of cis isomers of ß-carotene are not detected in the bloodstream, suggesting preferential absorption of the all-trans isomer of nutrients possessing provitamin A activity [52].

5. Role of tomato carotenoids in chronic disease prevention

Consumption of fruits and vegetables with beneficial health properties has been exploited for their ability to treat or prevent several chronic diseases [60]. There is an inverse relationship between the balanced consumption of tomatoes and tomato-derived products and the incidence of chronic diseases such as CVDs and various forms of cancers. These beneficial effects are attributed to carotenoids and phenolic compounds, which have high antioxidant capacities [48].

5.1 Oxidative stress

Oxidative stress plays an essential pathophysiological role in various chronic diseases such as CVDs, diabetes, neurodegenerative diseases, and cancer [60]. Free radicals, or other reactive oxygen- or nitrogen-containing species, are responsible for oxidative stress [48]. Oxidative stress occurs when there is a relative excess of ROS when compared with antioxidants [61]. ROS are reduced oxygen metabolites characterized by strong oxidizing capabilities. They are deleterious to cells at high concentrations but at low concentrations, they play a major role in cellular signaling and function [62]. ROS are formed as a by-product of mitochondrial respiration or metabolic activities (such as breathing, digesting food, metabolizing alcohol and drugs, and turning fats into energy) or by enzymes, such as superoxide dismutase, glutathione peroxidase, catalase, peroxiredoxins, and myeloperoxidases [60, 63]. Cells possess complex biochemical and genetic mechanisms to maintain ROS at physiologically normal concentrations, and deregulation in this balance has detrimental health effects [61, 62]. This is because abnormally high ROS levels may attack certain biomolecules (DNA, RNA, proteins lipids, and carbohydrates) causing damage to cells, tissues, and organs. [64]. The continuous production of free radicals in humans must be equivalent to the rate of antioxidant intake/synthesis [60]. Molecules such as ascorbate, a-tocopherol, and carotenoids are examples of antioxidants that are capable of quenching ROS. The structural properties of carotenoid molecules, particularly the presence of conjugated carbon–carbon double bonds enable the quenching of ROS and subsequently a reduction in ROS levels [18]. Tomato and related products contain carotenoids, particularly lycopene, one of the most potent antioxidants that have been found to protect against these chronic diseases by mitigating oxidative damage and improving the oxidative status [19, 48, 65]. Lycopene exerts strong antioxidant activity because it contains many double-conjugated bonds (11 conjugated double bonds and two unconjugated double bonds), which explains why lycopene can quench ROS and efficiently scavenge free radicals [7]. A study demonstrated that a long-term tomato-rich diet consisting of tomato juice, tomato sauce, tomato paste, ketchup, spaghetti sauce, and ready-to-serve tomato soup can reduce oxidative stress, this was attributed to an increase in serum lycopene levels from 181.79 ± 31.25 to 684.7 ± 113.91 nmol/l, as well as an increase in total antioxidant potential from 2.26 ± 0.015 to 2.38 ± 0.17 mmol/l Trolox equivalent [65]. The level of oxidative stress induced by in-vitro X-ray exposure in healthy adults was determined using serum 8-oxo-7, 8-dihydro-2-deoxyguanosine (8-oxo-dG), and plasma reactive oxygen metabolite-derived compounds (d-ROMs), the results suggested that continuous tomato juice consumption could decrease extracellular 8-oxo-dG and d-ROMs [66]. Previous studies have shown that tomato extracts containing 6% lycopene, other tomato carotenoids (phytoene and phytofluene above 1%, beta-carotene above 0.2%), can prevent oxidative stress-induced damage to fibroblast skin cells [67].

5.2 Tomato consumption and cardiovascular diseases

Worldwide, CVDs are an increasing concern due to the rising prevalence and consequent mortality and disability with a heavy economic burden since it is an important contributor to the cost of medical care [68, 69]. In 2019, 17.9 million people died from CVDs, representing 32% of all global deaths [70]. There is a growing body of epidemiological evidence that tomato and tomato products intake lower the risk of CVDs, through antioxidative, anti-inflammatory, and hypotensive effects [71]. The improvement of biomarkers associated with CVD development and the subsequent reduction in CVD risk has been ascribed to increased plasma lycopene levels. Moderate intake (2–4 servings) of tomato products such as soup, paste puree, juice, or any other tomato beverages, when consumed with the addition of dietary lipids, such as olive oil or avocados, leads to a rise in plasma carotenoids, particularly lycopene [72]. Dietary lycopene consumed as oil-based tomato products confers cardiovascular benefits. The consumption of ≥7 servings/week of tomato-based food products has been associated with a 30% reduction in CVD development in women [73]. Consumption of two glasses of tomato juice satisfies the recommended daily intake of lycopene (35 mg), [74]. **Table 4** shows the lycopene content of tomatoes and some frequently consumed tomato-derived products.

Epidemiological studies also suggest that the risk of myocardial infarction is lowered in individuals with higher lycopene content in adipose tissue. The EURAMIC (European community multicenter study on antioxidants, myocardial Infarction, and breast cancer) case–control study conducted in 10 European countries to assess the relations between antioxidant status and acute myocardial infarction, found lycopene concentration of adipose tissue to be independently protective against myocardial infarction [76]. A recent study by Cheng et al. [77] reported that higher intakes of lycopene or its high serum concentrate have been associated with significant reductions in the risk of stroke (26%) and CVDs (14%). Another carotenoid present in processed tomato products associated with CVD risk reduction is β-carotene [78].

Product	Lycopene (mg/100 g)
Fresh tomatoes	0.72–20
Tomato juice	5–11.60
Tomato puree	16.67–34.7
Tomato paste	5.40–150.00
Ketchup	9.90–17.00

Adapted from [72, 74, 75].

Table 4.
Lycopene content of tomatoes and processed tomato products.

Low levels of high-density lipoprotein (HDL) cholesterol and elevated LDL cholesterol are established CVD risk factors [79]. Pharmacological therapies aimed at LDL lowering have convincingly proven to reduce CVD disorders, such as coronary heart disease. Therefore, LDL cholesterol levels should be lowered as much as possible to prevent CVD [80, 81]. Lycopene may modulate the expression of adhesion molecules in human vascular endothelial cells and increase the expression of LDL receptors involved in the regulation of cholesterol metabolism [75]. Increasing the concentration of HDL can slow and even reverse the progression of coronary atherosclerosis (coronary heart disease) and reduce CVD risk in those with dyslipidemia (abnormal levels of blood lipids including cholesterol). Consumption of two uncooked tomatoes per day demonstrated a significant elevation of HDL levels in overweight women [79]. Michaličková et al. [71] conducted a randomized controlled study to examine the effect of tomato juice on LDL cholesterol. The intervention group was supplemented with 200 g of tomato juice for 4 weeks and a significant reduction in total cholesterol and LDL was observed [71] indicating that tomato and derivatives have favorable effects on lipid metabolism.

Systemic arterial hypertension is a condition in which an individual has abnormally high blood pressure (BP) and is a primary risk factor for CVDs [82]. BP above 140 mmHg systolic and/or 90 mmHg diastolic is considered hypertensive [83]. Several studies indicated that tomato products intake leads to a significant reduction in BP [84, 85]. A higher dosage of tomato-derived supplements (containing more than 12 mg lycopene per day) could significantly lower systolic blood pressure (SBP), particularly among populations with baseline SBP > 120 mmHg [84]. The effect of treatments with tomato nutrient complexes (containing 5, 15, and 30 mg lycopene) was compared with 15 mg of synthetic lycopene and a placebo over 8 weeks, significant reductions in mean SBP were noted in tomato nutrient complexes treatments with 15 or 30 mg of lycopene [86]. A recent trial highlighted the benefits of processed tomato products on BP management in overweight middle-aged adults. A lowered diastolic BP was observed in participants that consumed a high tomato diet consisting of approximately 200 g/day or 1400 g/week of tomato products [78]. In a quasi-experimental study, 32 type 2 diabetes patients consumed 200 g raw tomato daily for 8 weeks. A significant decrease in systolic and diastolic BP was noted at the end of the study compared with initial values [87]. Tomato consumption might be beneficial for reducing CVD risk in type 2 diabetic patients.

5.3 Anti-cancer role of tomato carotenoids

The consumption of tomatoes and tomato-derived products is inversely related to the incidence of different types of cancers, (prostate, stomach, and lung cancers)

[7, 72, 88, 89]. A study on elderly patients in the US attributed a 50% reduction in mortality rates from cancer of all sites to a high intake of tomatoes [90]. Tomatoes and tomato products are typical components of the Mediterranean diet (MD). The MD represents a dietary pattern suitable for the prevention of chronic diseases [91]. A meta-analysis of observational studies, which evaluated the effects of the adoption of the MD on incidence and mortality of different types of cancer, showed that the high adherence to this diet was associated with a significantly lowered risk of overall cancer, especially colorectal cancer, pharyngeal and esophageal cancer, and prostate cancer [92]. The protective role of tomatoes is predominantly ascribed to the carotenoid, lycopene [93]. Researchers found that there was a lower rate of mortality from cancer in the group of US adults with the highest tomato and lycopene intake (42.5% and 45.9%, respectively) [94].

Extensive research has been conducted on the role of lycopene in the prevention of prostate cancer, the second most frequent cancer (after lung cancer) diagnosed in men worldwide [7, 72, 95], with higher incidence and mortality observed in developed countries [96]. Findings from ecological and migrant studies suggest that the wide disparity in incidence rates of prostate cancer worldwide may be attributed to a "Westernized" diet and lifestyle in developed countries [97]. A study conducted in 2011 using DU145 cells (human prostate cancer cells), revealed that the proliferation of these cells was significantly inhibited by lycopene. The authors found that lycopene induced a reduction of the proliferation rate at concentrations of 15 and 25 μM, but not at physiological concentrations (>2 μM) [98]. The US health Professionals Follow-up Study investigated the relationship of various carotenoids and retinol consumption with the risk of prostate cancer. There was an inverse relationship between the estimated intake of lycopene and the risk of this cancer. This reduced incidence was not observed with any other carotenoid. A reduction in risk of almost 35% was observed for a consumption rate of 10 or more servings of tomato products per week, and the protective action was greater with more advanced or aggressive prostate cancer [95]. In a more recent study, there was an 18% lower risk of prostate cancer associated with adherence to the same recommended tomato intake [97].

Evidence pointing to the protective effect of tomato product consumption for other cancer sites other than the prostate is ambiguous [99]. Lung cancer is the leading cause of cancer death, with an estimated 1.8 million deaths (18%) [100]. Growing evidence suggests that tomato lycopene may be preventive against the development of this cancer [101]. In 2020, a study demonstrated that lycopene treatment may inhibit the growth of lung tumor cell line A549. Varying amounts of lycopene (2.5, 5, and 25 μL) were used to treat lung cancer cell cultures and higher lycopene concentrations were more damaging to cancer cell nuclei [102]. Among 14 case-control lung cancer studies, only 6 studies showed a statistically significant risk reduction for cancer incidence, averaging 51%. However, cohort studies showed no beneficial relation between lung cancer reduction and tomato product consumption [99]. According to epidemiological studies, higher lycopene intake is associated with either a reduced or no change in lung cancer risk when compared to lower intake levels [103]. Gastric (stomach) cancer remains one of the dominant causes of cancer mortality in the world [104, 105]. Tomato or lycopene intake has proven to reduce gastric cancer risk in a variety of populations [72, 95]. However, few studies have been conducted to date. A meta-analysis study consisting of 21 studies supports an inverse association between tomato consumption and risk of gastric cancer [106]. Previous research projects have reported a negative relationship between tomato intake and the risk of gastric cancer. A study conducted in Korea consisting of 1245 subjects (415 cases and 830 matched controls; 810 men and 435 women), highlighted that the consumption of tomatoes and tomato ketchup was inversely associated with GC risk in the overall subjects [107]. In a case-control study in Uruguay, tomato consumption had a strong inverse association with gastric carcinogenesis. The carotenoids, α-carotene, and lycopene were strongly associated with this reduction in stomach cancer development [108].

5.4 Tomato in protection against obesity and diabetes

The incidence of type 2 diabetes (diabetes mellitus) and obesity has increased worldwide during the last century in both developed and developing countries [109]. Obesity is a chronic inflammatory disorder in which an increase in circulating inflammatory mediators is caused by an increase in body fat [19, 110]. Destructive mechanisms associated with obesity increase ROS and hamper the antioxidant status [111]. Individuals having a fasting blood sugar level of 126 mg/dl or higher on 2 separate days, will be diagnosed with type 2 diabetes [112]. The strong link between type 2 diabetes and obesity [113], with 80 percent of type 2 diabetes patients being overweight [112], was named "diabesity." According to the WHO, overweight and obesity account for 44% of diabetes cases. Therefore, it is necessary to develop therapeutic strategies favoring weight loss and blood glucose control (anti-obesity and antidiabetic treatment) [114].

A randomized controlled clinical trial was conducted on 64 overweight or obese demonstrated that tomato juice reduces oxidative stress in overweight females and may prevent the development of obesity-related diseases. In this study, the antioxidant parameters of study participants that ingested 330 ml/day of tomato juice for 20 days were analyzed at the beginning and after this period verifying an increase in plasma total antioxidant capacity (TAC) and erythrocyte antioxidant enzymes [115]. Ghavipour et al. [110] demonstrated that tomato juice consumption lowers inflammation in overweight and obese females. The predictive biomarkers of inflammation [tumour necrosis factor-alpha (TNF-α) and interleukin 8 (IL-8)] were examined in study participants who drank 330 ml of tomato juice every day for 20 days. The serum levels of IL-8 and TNF- α were significantly lower in overweight people that consumed the tomato juice compared to the control group. The scientists concluded that eating more tomatoes may lower the risk of inflammatory disorders, such as CVDs and diabetes [110].

The goal of diabetes management is to maintain plasma glucose concentrations at near-normal levels [112]. According to the WHO, expected values for normal fasting blood glucose levels are between 70 mg/dl (3.9 mmol/l) and 100 mg/dl (5.6 mmol/l) [116]. Chemicals found in fresh or processed tomatoes have been shown to have antihyperglycemic properties that enable the lowering of glucose levels in the blood. In streptozotocin (STZ)-induced hyperglycemic rats, oral administration of tomato extract lycopene (90 mg/kg of body weight) resulted in a lower serum glucose level. The therapeutic amount of lycopene in humans is around 14.5 mg/kg of body weight. Lycopene's anti-diabetic properties may be linked to its antioxidant activity, which reduces the number of free radicals generated [117]. Another study indicated that fasting blood sugar levels decreased after drinking tomato juice for 3 weeks [112]. The reduction in fasting blood glucose levels was found to be an average of 9.00 mg/dl (7.64%). Supplementation with β-carotene did not affect type 2 diabetes in randomized controlled trials [118, 119]. The impact of lycopene consumption on blood glucose concentration was analyzed, each 1 mg increase in lycopene consumption was associated with a 0·005 mmol/l decrease in fasting blood glucose concentration [120]. The effects of pre-prandial tomato intake on body weight, fat percentage, triglyceride, cholesterol, and blood sugar levels were evaluated in 35 young women aged 18 to 21 years. Participants ate raw, ripe tomatoes (90 g) before lunch each day for 4 weeks. At the end of the study, there were significant reductions in body weight (1.09 ± 0.12 kg), fat % (1.54 ± 0.52%), fasting blood glucose (5.29 ± 0.80 mg/dl), triglycerides (8.31 ± 1.34 mg), and cholesterol (10.17 ± 1.21 mg/dl). Thus, tomato consumption before meals was positively correlated with body weight, fat %, triglycerides, blood sugar, and cholesterol levels in young adult women [121].

6. Conclusion

Tomato is a food product available all year round and is highly consumed by populations around the world. Tomato carotenoids have demonstrated antioxidant and protective effects against chronic diseases. Among these carotenoids, lycopene, in particular, has shown distinct antioxidant and anticancer properties at cellular levels. Numerous studies highlighted the potential benefits of tomato carotenoids in delaying or preventing the development of chronic degenerative diseases. Nevertheless, further research is required to better elucidate the beneficial health effects of these carotenoids as well as their precise modes of action in the risk reduction of chronic diseases. Considering the reported positive implications of tomatoes and their products in chronic disease prevention, dietary intake of naturally occurring carotenoid-rich tomato and processed tomato products should be highlighted and recommended.

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References

[1] Bergougnoux V. The history of tomato: From domestication to biopharming. Biotechnology Advances. 2014;**32**(1):170-189. DOI: 10.1016/j.biotechadv.2013.11.003

[2] Kimura S, Sinha N. Tomato (*Solanum lycopersicum*): A model fruit-bearing crop. Cold Spring Harbor Protocols. 2008;**3**:1-9. DOI: 10.1101/pdb.emo105

[3] Villanueva EE. An Overview of Recent Studies of Tomato (*Solanum lycopersicum* spp.) from a Social, Biochemical and Genetic Perspective on Quality Parameters [Introductory Paper]. Alnarp-Sweden: Swedish University of Agricultural Sciences; 2018

[4] Noonari S, Solangi SU, Laghari MA, Wagan SA, Sethar AA, Kalwar GY, et al. Economic implications of tomato production in Naushahro Feroze District of Sindh Pakistan. Research on Humanities and Social Sciences. 2015;**5**:158-170

[5] Quinet M, Angosto T, Yuste-Lisbona FJ, Blanchard-Gros R, Bigot S, Martinez JP, et al. Tomato fruit development and metabolism. Frontiers in Plant Science. 2019;**10**(1554):1-23. DOI: 10.3389/fpls.2019.01554

[6] Food and Agriculture Organization (FAO). FAOSTAT: Crops and Livestock Products [Internet]. 2022. Available from: https://www.fao.org/faostat/en/#data/QCL/visualize [Accessed: 26 January 2022]

[7] Martí R, Roselló S, Cebolla-Cornejo J. Tomato as a source of carotenoids and polyphenols targeted to cancer prevention. Cancers. 2016;**8**(58):2-28. DOI: 10.3390/cancers8060058

[8] Stajčić S, Ćetković G, Čanadanović-Brunet J, Djilas SM, Mandic AI, Četojević-Simin DD. Tomato waste: Carotenoids content, antioxidant and cell growth activities. Food Chemistry. 2015;**172**:225-232. DOI: 10.1016/j.foodchem.2014.09.069

[9] Carotene.org. Carotenoids – An Overview [Internet]. 2022. Available from: https://www.carotene.org/carotenoids/ [Accessed: 26 January 2022]

[10] Britton G, Liaaen-Jensen S, Pfander H, editors. Carotenoids Handbook. 1st ed. Basel: Birkhauser Verlag; 2004. p. 885. DOI: 10.1007/978-3-0348-7836-4

[11] Ruiz-Sola MÁ, Rodríguez-Concepción M. Carotenoid biosynthesis in Arabidopsis: A colorful pathway. Arabidopsis Book. 2012;**10**:1-28. DOI: 10.1199/tab. 0158

[12] Swapnil P, Meena M, Singh SK, Dhuldhaj UP, Marwal A. Vital roles of carotenoids in plants and humans to deteriorate stress with its structure, biosynthesis, metabolic engineering and functional aspects. Current Plant Biology. 2021;**26**:1-11. DOI: 10.1016/j.cpb.2021.100203

[13] Maoka T. Carotenoids as natural functional pigments. Journal of Natural Medicines. 2020;**74**:1-16. DOI: 10.1007/s11418-019-01364-x

[14] Delgado-Vargas F, Jiménez AR, Paredes-López O. Natural pigments: Carotenoids, anthocyanins, and betalains - characteristics, biosynthesis, processing, and stability. Critical Reviews in Food Science and Nutrition. 2000;**40**(3):173-289. DOI: 10.1080/10408690091189257

[15] Maoka T. Carotenoids in marine animals. Marine Drugs. 2011;**9**(2): 278-293. DOI: 10.3390/md9020278

[16] Eldahshan OA, Singab ANB. Carotenoids. Journal of Pharmacognosy and Phytochemistry. 2013;2(1):225-234

[17] Prakash D, Gupta C. Carotenoids: Chemistry and health benefits. In: Prakash D, Sharma G, editors. Phytochemicals of Nutraceutical Importance. 1st ed. Wallingford: CAB International publishing; 2014. pp. 181-195. DOI: 10.1079/9781780643632.0181

[18] Bakan E, Akbulut ZT, Inanç AL. Carotenoids in foods and their effects on human health. Akademik Gıda. 2014;**12**(2):61-68

[19] Pinela J, Oliveira MBPP, Ferreira ICFR. Bioactive compounds of tomatoes as health promoters. In: Silva LR, Silva BM, editors. Natural Bioactive Compounds from Fruits and Vegetables. 2nd ed. Sharjah: Bentham Science Publishers; 2016. pp. 48-91. DOI: 10.2174/97816810824311160101

[20] Elvira-Torales LI, García-Alonso J, Periago-Castón MJ. Nutritional importance of carotenoids and their effect on liver health: A review. Antioxidants (Basel). 2019;**8**(7):229-252. DOI: 10.3390/antiox8070229

[21] Jaswir I, Noviendri D, Hasrini RF, et al. Carotenoids: Sources, medicinal properties and their application in food and nutraceutical industry. Journal of Medicinal Plants Research. 2011;**5**:7119-7131. DOI: 10.5897/JMPRX11.011

[22] Thomas SE, Johnson EJ. Xanthophylls. Advances in Nutrition. 2018;**9**(2):160-162. DOI: 10.1093/advances/nmx005

[23] Rodriguez-Amaya DB, Kimura M. HarvestPlus Handbook for Carotenoid Analysis. 1st ed. Washington, DC: International Food Policy Research Institute; 2004. p. 63

[24] Sartori AGO, Silva MV. Main food sources of carotenoids, according to the purpose and degree of processing, for beneficiaries of the 'Bolsa Família' in Brazil. Food Science and Technology. 2014;**34**(2):408-415. DOI: 10.1590/fst.2014.0056

[25] Flores P, Sánchez E, et al. Genotypic variability of carotenoids in traditional tomato cultivars. Food Research International. 2017;**100**(Pt 3):510-516. DOI: 10.1016/j.foodres.2016.07.014

[26] Tanumihardjo SA. Carotenoids: Health effects. In: Caballero B, editor. Encyclopedia of Human Nutrition. 3rd ed. Cambridge: Academic Press; 2013. p. 292-297. DOI: 10.1016/B978-0-12-375083-9.00045-3

[27] Orsi B, Sestari I, Preczenhak AP, et al. Allelic variations in the tomato carotenoid pathway lead to pleiotropic effects on fruit ripening and nutritional quality. Postharvest Biology and Technology. 2021;181(111632):1-11. DOI: 10.1016/j.postharvbio.2021.111632

[28] Shi J, Kakuda Y, Yeung D. Antioxidative properties of lycopene and other carotenoids from tomatoes: Synergistic effects. BioFactors. 2004;**21**(1-4):203-210. DOI: 10.1002/biof.552210141

[29] Guil-Guerrero JL, Rebolloso-Fuentes MM. Nutrient composition and antioxidant activity of eight tomato (*Lycopersicon esculentum*) varieties. Journal of Food Composition and Analysis. 2009;**22**:123-129. DOI: 10.1016/j.jfca.2008.10.012

[30] Kotikova Z, Hejtmánková A, Jaromir L. Determination of the influence of variety and level of maturity on the content and development of carotenoids in tomatoes. Czech Journal of Food Sciences. 2009;**27**:200-203. DOI: 10.17221/1093-CJFS

[31] Inbaraj B, Bing-Huei C. Carotenoids in tomato plants. In: Preedy VR, Watson RR, editors. Tomatoes and Tomato Products. 1st ed. Boca Raton: CRC Press; 2008. pp. 133-164. DOI: 10.1201/9781439843390-7

[32] Dzakovich MP, Gas-Pascual E, Orchard CJ, et al. Analysis of Tomato Carotenoids: Comparing Extraction and Chromatographic Methods. Journal of AOAC International. 2019;102:1069-1079. DOI: 10.5740/jaoacint.19-0017

[33] Abushita AA, Daood HG, Biacs PA. Change in carotenoids and antioxidant vitamins in tomato as a function of varietal and technological factors. Journal of Agricultural and Food Chemistry. 2000;**48**(6):2075-2081. DOI: 10.1021/jf990715p

[34] Del Giudice R, Petruk G, Raiola A, et al. Carotenoids in fresh and processed tomato (*Solanum lycopersicum*) fruits protect cells from oxidative stress injury. Journal of the Science of Food and Agriculture. 2016;**97**(5):1616-1623. DOI: 10.1002/jsfa.7910

[35] Raiola A, Rigano MM, Calafiore R, Frusciante L, Barone A. Enhancing the health-promoting effects of tomato fruit for biofortified food. Mediators of Inflammation. 2014;**2014**:1-16. DOI: 10.1155/2014/139873

[36] Olmedilla-Alonso B, Rodríguez-Rodríguez E, et al. Dietary β-cryptoxanthin and α-carotene have greater apparent bioavailability than β-carotene in subjects from countries with different dietary patterns. Nutrients. 2020;**12**(9):2639. DOI: 10.3390/nu12092639

[37] Nagarajan J, Ramanan RN, Raghunandan ME, et al. Carotenoids. In: Galanakis CM, editor. Nutraceutical and Functional Food Components: Effects of Innovative Processing Techniques. 1st ed. Amsterdam: Elsevier Inc; 2017. pp. 259-296. DOI: 10.1016/B978-0-12-805257-0.00008-9

[38] Gama J, Tadiotti A, Sylos C. Comparison of carotenoid content in tomato, tomato pulp and ketchup by liquid chromatography. Alimentos e Nutrição. 2009;**17**(4):353-358

[39] Schieber A, Weber F. Carotenoids. In: Carle R, Schweiggert R, editors. Handbook on Natural Pigments in Food and Beverages. Industrial Applications for Improving Food Color. 1st ed. Sawston: Woodhead Publishing; 2016. pp. 101-123. DOI: 10.1016/B978-0-08-100371-8.00005-1

[40] Vallverdú-Queralt A, Regueiro J, et al. Carotenoid profile of tomato sauces: Effect of cooking time and content of extra virgin olive oil. International Journal of Molecular Sciences. 2015;**16**(5):9588-9599. DOI: 10.3390/ijms16059588

[41] Schulz H, Schütze W, Baranska M. Fast determination of carotenoids in tomatoes and tomato products by Raman spectroscopy. Acta Horticulturae. 2006;**712**:901-905. DOI: 10.17660/ActaHortic.2006.712.118

[42] D'Evoli L, Lombardi-Boccia G, Lucarini M. Influence of heat treatments on carotenoid content of cherry tomatoes. Food. 2013;**2**(3):352-363. DOI: 10.3390/foods2030352

[43] Mendelová A, Fikselová M, Mendel Ľ. Carotenoids and lycopene content in fresh and dried tomato fruits and tomato juice. Acta Universitatis Agriculturae Et Silviculturae Mendelianae Brunensis. 2013;**61**(5):1329-1337. DOI: 10.11118/actaun201361051329

[44] Kerkhofs NS, Lister CE, Savage GP. Change in colour and antioxidant content

of tomato cultivars following forced-air drying. Plant Foods for Human Nutrition. 2005;**60**:117-121. DOI: 10.1007/s11130-005-6839-8

[45] Zanoni B, Peri C, Nani R, Lavelli V. Oxidative heat damage of tomato halves as affected by drying. Food Research International. 1999;**31**(5):395-394. DOI: 10.1016/s0963-9969(98)00102-1

[46] Shi J, Le Maguer M, Kakuda Y, et al. Lycopene degradation and isomerisation in tomato dehydration. Food Research International. 1999;**32**(1):15-21. DOI: 10.1016/S0963-9969(99)00059-9

[47] Lavelli V, Hippeli S, Peri C, et al. Evaluation of radical scavenging activity of fresh and air-dried tomatoes by three model reactions. Journal of Agricultural and Food Chemistry. 1999;**47**(9):3826-3831. DOI: 10.1021/jf981372i

[48] Szabo K, Catoi AF, Vodnar DC. Bioactive compounds extracted from tomato processing by-products as a source of valuable nutrients. Plant Foods for Human Nutrition. 2018;**73**(4):268-277. DOI: 10.1007/s11130-018-0691-0

[49] Hammond BR, Renzi LM. Carotenoids. Advances in Nutrition. 2013;**4**(4):474-476. DOI: 10.3945/an.113.004028

[50] Deming D, Erdman J. Mammalian carotenoid absorption and metabolism. Pure and Applied Chemistry. 1999;**71**(12):2213-2223. DOI: 10.1351/pac199971122213

[51] Brown MJ, Ferruzzi MG, Nguyen ML, et al. Carotenoid bioavailability is higher from salads ingested with full-fat than with fat-reduced salad dressings as measured with electrochemical detection. The American Journal of Clinical Nutrition. 2004;**80**(2):396-403. DOI: 10.1093/ajcn/80.2.396 PMID: 15277161

[52] Kopec RE. Bioavailability, Metabolism, and Bioefficacy of Tomato Carotenoids [Thesis]. Columbus: Ohio State University; 2012

[53] Górecka D, Wawrzyniak A, et al. Lycopene in tomatoes and tomato products. Open Chemistry. 2020;**18**(1):752-756. DOI: 10.1515/chem-2020-0050

[54] Saad AG, Pék Z, et al. Determination of carotenoids in tomato products using Vis/Nir spectroscopy. The Journal of Microbiology, Biotechnology and Food Sciences. 2017;**7**(1):27-31. DOI: 10.15414/jmbfs.2017.7.1.27-31

[55] Shi J, Le Maguer M. Lycopene in tomatoes: Chemical and physical properties affected by food processing, Critical Reviews in Food Science and Nutrition. 2000;**40**(19):1-42, DOI: 10.1080/10408690091189275

[56] van het Hof KH, de Boer BC, Tijburg LB, et al. 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. The Journal of Nutrition. 2000;**130**(5):1189-1196. DOI: 10.1093/jn/130.5.1189

[57] Lin CH, Chen BH. Determination of carotenoids in tomato juice by liquid chromatography. Journal of Chromatography A. 2003;**1012**(1):103-109. DOI: 10.1016/S0021-9673(03)01138-5

[58] Lin CH, Chen BH. Stability of carotenoids in tomato juice during storage. European Food Research and Technology. 2005;**221**:274-280. DOI: 10.1007/s00217-005-1155-y

[59] Strati I, Vasso O. Recovery and isomerization of carotenoids from

tomato processing by-products. Waste and Biomass Valorization. 2016;7:843-850. DOI: 10.1007/s12649-016-9535-z

[60] Sharifi-Rad M, Kumar NVA, et al. Lifestyle, oxidative stress, and antioxidants: Back and forth in the pathophysiology of chronic diseases. Frontiers in Physiology. 2020;**11**(649):1-21. DOI: 10.3389/fphys.2020.00694

[61] Hayes JD, Dinkova-Kostova AT, Tew KD. Oxidative stress in cancer. Cancer Cell. 2020;**38**(2):167-197. DOI: 10.1016/j.ccell.2020.06.001

[62] Arfin S, Jha NK, Jha SK, et al. Oxidative stress in cancer cell metabolism. Antioxidants (Basel). 2021;**10**(642):1-28. DOI: 10.3390/antiox10050642

[63] Dubois-Deruy E, Peugnet V, et al. Oxidative stress in cardiovascular diseases. Antioxidants. 2020;**9**(864):1-15. DOI: 10.3390/antiox9090864

[64] Engwa GA, EnNwekegwa FN, et al. Free radicals, oxidative stress-related diseases and antioxidant supplementation. Alternative Therapies in Health and Medicine. 2020;AT6236

[65] Rao AV. Processed tomato products as a source of dietary lycopene: Bioavailability and antioxidant properties. Canadian Journal of Dietetic Practice and Research. 2004;**65**(4): 161-165. DOI: 10.3148/65.4.2004.161

[66] Nakamura A, Itaki C, Saito A, et al. Possible benefits of tomato juice consumption: A pilot study on irradiated human lymphocytes from healthy donors. Nutrition Journal. 2017;**16**(27): 1-11. DOI: 10.1186/s12937-017-0248-3

[67] Darawsha A, Trachtenberg A, Levy J, et al. The protective effect of carotenoids, polyphenols, and Estradiol on dermal fibroblasts under oxidative stress. Antioxidants. 2021;**10**(12):2023. DOI: 10.3390/antiox10122023

[68] Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: Results from global burden of disease study 2017. BMC Public Health. 2021;**21**(401):1-12. DOI: 10.1186/s12889-021-10429-0

[69] Roth GA, Mensah GA, Johnson CO, et al. global burden of cardiovascular diseases and risk factors, 1990-2019: Update from the GBD 2019 study. Journal of the American College of Cardiology. 2020;**76**(25):2982-3021. DOI: 10.1016/j.jacc.2020.11.010

[70] World Health Organization (WHO). Cardiovascular Diseases (CVDs) [Internet]. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [Accessed: 29 January 2022]

[71] Michaličková D, Belović M, Ilić N, et al. Comparison of polyphenol-enriched tomato juice and standard tomato juice for cardiovascular benefits in subjects with stage 1 hypertension: A randomized controlled study. Plant Foods for Human Nutrition;**74**:122-127. DOI: 10.1007/s11130-019-0714-5

[72] Marques C, Lima M, Oliveira J, et al. Tomato lycopene: Functional proprieties and health benefits. World Academy of Science, Engineering and Technology, International Journal of Agricultural and Biosystems Engineering. 2015;**9**(10): 1089-1099. DOI: 10.5281/zenodo.1109297

[73] Sesso HD, Liu S, Gaziano JM, Buring JE. Dietary lycopene, tomato-based food products and cardiovascular disease in women. The Journal of Nutrition. 2003;**133**(7):2336-2341. DOI: 10.1093/jn/133.7.2336

[74] Basuny MAM. The anti-atherogenic effects of lycopene. In: Frank S, Kostner G, editors. Lipoproteins - Role in Health and Diseases. London: IntechOpen; 2012. pp. 489-506. DOI: 10.5772/48134

[75] Thies F, Masson LF, Rudd A, et al. Effect of a tomato-rich diet on markers of cardiovascular disease risk in moderately overweight, disease-free, middle-aged adults: A randomized controlled trial. The American Journal of Clinical Nutrition 2012;95(5):1013-1022. DOI: 10.3945/ajcn.111.026286

[76] Willcox JK, Catignani GL, Lazarus S. Tomatoes and cardiovascular health. Critical Reviews in Food Science and Nutrition. 2003;**43**(1):1-18. DOI: 10.1080/10408690390826437

[77] Cheng HM, Koutsidis G, Lodge JK, et al. Lycopene and tomato and risk of cardiovascular diseases: A systematic review and meta-analysis of epidemiological evidence. Critical Reviews in Food Science and Nutrition. 2019;**59**(1):141-158. DOI: 10.1080/10408398.2017.1362630

[78] Burton-Freeman B, Edirisinghe I, et al. Processed tomato products and risk factors for cardiovascular disease. Nutrition and Aging. 2015;**3**(2-4):193-201. DOI: 10.3233/NUA-150059

[79] Cuevas-Ramos D, Almeda-Valdés P, et al. Effect of tomato consumption on high-density lipoprotein cholesterol level: A randomized, single-blinded, controlled clinical trial. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2013;**6**:263-273. DOI: 10.2147/DMSO.S48858

[80] Rizvi AA, Stoian AP, Janez A, Rizzo M. Lipoproteins and cardiovascular disease: An update on the clinical significance of atherogenic small, dense LDL and new therapeutical options. Biomedicine. 2021;**9**(1579):1-7. DOI: 10.3390/biomedicines9111579

[81] Bantwal G, George B. Low density lipoprotein cholesterol target: Changing goal posts. Indian Journal of Endocrinology and Metabolism. 2012;**16**(Suppl. 2):233-235. DOI: 10.4103/2230-8210.104047

[82] Oparil S, Acelajado MC, Bakris GL, et al. Hypertension. Nature Reviews Disease Primers. 2018;**4**(18014):1-53. DOI: 10.1038/nrdp.2018.14

[83] Tan JL, Thakur K. Hypertension, Systolic. 1st ed. Treasure Island: StatPearls Publishing; 2018. p. 11

[84] Li X, Xu J. Lycopene supplement and blood pressure: An updated meta-analysis of intervention trials. Nutrients. 2013;**5**(9):3696-3712. DOI: 10.3390/nu5093696

[85] Ried K, Fakler P. Protective effect of lycopene on serum cholesterol and blood pressure: Meta-analyses of intervention trials. Maturitas. 2011;**68**(4):299-310. DOI: 10.1016/j.maturitas.2010.11.018

[86] Wolak T, Sharoni Y, Levy J, et al. Effect of tomato nutrient complex on blood pressure: A double blind. Randomized Dose-Response Study. Nutrients. 2019;**11**(950):1-13. DOI: 10.3390/nu11050950

[87] Shidfar F, Froghifa N, Vafa M, et al. The effects of tomato consumption on serum glucose, apolipoprotein B, apolipoprotein A-I, homocysteine and blood pressure in type 2 diabetic patients. International Journal of Food Sciences and Nutrition. 2011;**62**(3):289-294. DOI: 10.3109/09637486.2010.529072

[88] Giovannucci E, Ascherio A, Rimm EB, et al. Intake of carotenoids

and retinol in relation to risk of prostate cancer. Journal of the National Cancer Institute. 1995;**87**(23):1767-1776. DOI: 10.1093/jnci/87.23.1767

[89] Rawla P. Epidemiology of prostate cancer. World Journal of Oncology. 2019;**10**(2):63-89. DOI: 10.14740/wjon1191

[90] Colditz GA, Branch LG, Lipnick RJ, et al. Increased green and yellow vegetable intake and lowered cancer deaths in an elderly population. The American Journal of Clinical Nutrition. 1985;**41**:32-36. DOI: 10.1093/ajcn/41.1.32

[91] Sofi F, Fabbri A, Casini A. Inflammation and Cardiovascular Disease and Protection by the Mediterranean Diet. In: Romagnolo DF, Selmin OI, editors. Mediterranean Diet. Dietary Guidelines and Impact on Health and Disease. 1st ed. Switzerland: Springer International Publishing; 2016. pp. 89-96

[92] Schwingshackl L, Hoffmann G. Adherence to Mediterranean diet and risk of cancer: A systematic review and meta-analysis of observational studies. International Journal of Cancer. 2014;**135**:1884-1897. DOI: 10.1002/ijc.28824

[93] Denniss SG, Haffner TD, Kroetsch JT, et al. Effect of short-term lycopene supplementation and postprandial dyslipidemia on plasma antioxidants and biomarker of endothelial health in young healthy individuals. Vascular Health and Risk Management. 2008;**4**:213-222. DOI: 10.2147/vhrm.2008.04.01.213

[94] Mazidi M, Ferns GA, Banach M. A high consumption of tomato and lycopene is associated with a lower risk of cancer mortality: Results from a multi-ethnic cohort. Public Health Nutrition. 2020;**23**(9):1569-1575. DOI: 10.1017/S1368980019003227

[95] Giovannucci E. Tomatoes, tomato-based products, lycopene, and cancer: Review of the epidemiologic literature. Journal of the National Cancer Institute. 1999;**91**(4):317-331. DOI: 10.1093/jnci/91.4.317

[96] Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. International Journal of Cancer. 2010;**127**(12):2893-2917. DOI: 10.1002/ijc.25516

[97] Hassanipour-Azgomi S, Mohammadian-Hafshejani A, Ghoncheh M, Towhidi F, Jamehshorani S, Salehiniya H. Incidence and mortality of prostate cancer and their relationship with the Human Development Index worldwide. Prostate International. 2016;**4**(3):118-124. DOI: 10.1016/j.prnil.2016.07.001

[98] Ford NA, Elsen AC, Zuniga K, et al. Lycopene and apo-12′-lycopenal reduce cell proliferation and alter cell cycle progression in human prostate cancer cells. Nutrition and Cancer. 2011;**63**(2):256-263. DOI: 10.1080/01635581.2011.523494

[99] Hwang ES, Bowen PE. Can the consumption of tomatoes or lycopene reduce cancer risk? Integrative Cancer Therapies. 2002;**1**(2):121-132. DOI: 10.1177/1534735402001002003

[100] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;**71**(3):209-249. DOI: 10.3322/caac.21660

[101] Palozza P, Simone RE, et al. Tomato lycopene and lung cancer prevention: From experimental to human studies. Cancers. 2011;**3**(2):2333-2357. DOI: 10.3390/cancers3022333

[102] Pogoda K, Pucka M, Tabarkiewicz J, et al. Lycopene activity on lung and kidney cancer cells by T2 relaxation time 1H magnetic resonance imaging in vitro. European Journal of Clinical and Experimental Medicine. 2020;**18**(1):5-9. DOI: 10.15584/ejcem.2020.1.1

[103] Bacanli M, Başaran N, Başaran AA. Lycopene: Is it beneficial to human health as an antioxidant? Turkish Journal Of Pharmaceutical Sciences. 2017;**14**(3): 311-318. DOI: 10.4274/tjps.43043

[104] Crew KD, Neugut AI. Epidemiology of gastric cancer. World Journal of Gastroenterology. 2006;**12**(3):354-362. DOI: 10.3748/wjg.v12.i3.354

[105] Tsugane S, Sasazuki S. Diet and the risk of gastric cancer: Review of epidemiological evidence. Gastric Cancer. 2007;**10**(2):75-83. DOI: 10.1007/s10120-007-0420-0

[106] Yang T, Yang X, et al. The role of tomato products and lycopene in the prevention of gastric cancer: A meta-analysis of epidemiologic studies. Medical Hypotheses. 2013;**80**:383-388. DOI: 10.1016/j.mehy.2013.01.005

[107] Kim JH, Lee J, Choi IJ, et al. Dietary carotenoids intake and the risk of gastric cancer: A case-control study in Korea. Nutrients. 2018;**10**(8):1031. DOI: 10.3390/nu10081031

[108] De Stefani E, Boffetta P, Brennan P, et al. Dietary carotenoids and risk of gastric cancer: A case-control study in Uruguay. European Journal of Cancer Prevention. 2000;**9**(5):329-334. DOI: 10.1097/00008469-200010000-00007

[109] Serván PR. Obesity and diabetes. Nutricion Hospitalaria. 2013; **28**(Suppl. 5):138-143. DOI: 10.3305/nh.2013.28.sup5.6929

[110] Ghavipour M, Saedisomeolia A, Djalali M, et al. Tomato juice consumption reduces systemic inflammation in overweight and obese females. British Journal of Nutrition. 2013;**109**(11):2031-2035. DOI: 10.1017/S0007114512004278

[111] Pourahmadi Z, Mahboob S, Saedisomeolia A, et al. The effect of tomato juice consumption on antioxidant status in overweight and obese females. Women & Health. 2015;**55**(7):795-804. DOI: 10.1080/03630242.2015.1050546

[112] Tarigan H, Marlina S, et al. The Impact of Tomato Juice on Reducing Blood Sugar Levels at Diabetes Mellitus Patients, Proceedings of the International Conference on Health Informatics and Medical Application Technology (ICHIMAT 2019); 6-8 November 2019. Medan. Setúbal: SCITEPRESS; 2020. pp. 270-277

[113] Fagot-Campagna A, Balkau B, Simon D, et al. High free fatty acid concentration: An independent risk factor for hypertension in the Paris prospective study. International Journal of Epidemiology. 1998;**27**(5):808-813. DOI: 10.1093/ije/27.5.808

[114] Leitner DR, Frühbeck G, Yumuk V, et al. Obesity and type 2 diabetes: Two diseases with a need for combined treatment strategies - EASO can lead the way. Obesity Facts. 2017;**10**(5):483-492. DOI: 10.1159/000480525

[115] Ghavipour M, Sotoudeh G, Ghorbani M. Tomato juice consumption improves blood antioxidative biomarkers in overweight and obese females. Clinical Nutrition. 2015;**34**(5):805-809. DOI: 10.1016/j.clnu.2014.10.012

[116] World Health Organization. Mean fasting blood glucose [Internet]. 2022. Available from: https://www.who.int/

data/gho/indicator-metadata-registry/imr-details/2380 [Accessed: 30 January 2022]

[117] Banihani SA. Tomato (*Solanum lycopersicum L.*) and type 2 diabetes. International Journal of Food Properties. 2018;**21**(1):99-105. DOI: 10.1080/10942912.2018.1439959

[118] Song Y, Cook NR, Albert CM, et al. Effects of vitamins C and E and beta-carotene on the risk of type 2 diabetes in women at high risk of cardiovascular disease: A randomized controlled trial. The American Journal of Clinical Nutrition. 2009;**90**(2):429-437. DOI: 10.3945/ajcn.2009.27491

[119] Kataja-Tuomola M, Sundell JR, Mannisto S, et al. Effect of alpha-tocopherol and beta-carotene supplementation on the incidence of type 2 diabetes. Diabetologia. 2008;**51**:47-53. DOI: 10.1007/s00125-007-0864-0

[120] Gao Q, Zhong C, Zhou X, et al. The association between intake of dietary lycopene and other carotenoids and gestational diabetes mellitus risk during mid-trimester: A cross-sectional study. British Journal of Nutrition. 2019;**121**(12):1405-1412. DOI: 10.1017/S0007114519000606

[121] Vinha AF, Barreira SVP, Costa ASG, et al. Pre-meal tomato (*Lycopersicon esculentum*) intake can have anti-obesity effects in young women? International Journal of Food Sciences and Nutrition. 2014;**65**(8):1019-1026. DOI: 10.3109/09637486.2014.950206