



Bioactive compounds in tomato and their roles in disease prevention

Kabita Kumari Shah ^{1*}, Bindu Modi ², Bibek Lamsal ¹, Jiban Shrestha ³, Surya Prasad Aryal ⁴

¹Institute of Agriculture and Animal Science, Gokuleshwor College, Tribhuvan University, Baitadi, Nepal

²Central Department of Chemistry, Tribhuvan University, Kathmandu, Nepal

³National Plant Breeding and Genetics Research Centre, Nepal Agricultural Research Council, Khumaltar, Lalitpur, Nepal

⁴University of Kentucky, Lexington, Kentucky, USA

ARTICLE INFORMATION

Article History

Submitted: 19 Sep 2020

Accepted: 19 Nov 2020

First online: 30 Jun 2021

Academic Editor

Mohammad Golam Mostofa
mostofa@bsmrau.edu.bd

*Corresponding Author

Kabita Kumari Shah
agri.kabita35@gmail.com



ABSTRACT

Tomato (*Lycopersicon esculentum* L.) is an excellent source of many nutrients and secondary metabolites that are important for human health. Its fruits are rich in antioxidant compounds, which are important for human metabolism. Lycopene is one of the abundantly occurring antioxidants found in tomato. Lycopene is beneficial in preventing various chronic diseases such as cancer, cardiovascular diseases etc. Tomato is an important source of bioactive compounds which have antioxidant, anti-mutagenic, anti-proliferative, anti-inflammatory and anti-atherogenic activities. A group of vitamins (ascorbic acid and vitamin A), phenolic compounds (phenolic acids and flavonoids), carotenoids (lycopene, α , and β carotene), and glycoalkaloids (tomatine) are found in tomato. These compounds can provide protection to our health by neutralizing free radicals which are responsible for the growth of a range of degenerative diseases. The present review provides collective information on the pharmacological actions and chemistry of bioactive compounds (carotenoids, lycopene, β -carotene, lutein, and vitamins) found in tomato along with discussing possible health benefits.

Keywords: Antioxidant, bioactive compounds, carotenoids, lycopene, pharmacology, tomato



Cite this article: Shah KK, Modi B, Lamsal B, Shrestha J, Aryal SP. 2021. Bioactive compounds in tomato and their roles in disease prevention. *Fundamental and Applied Agriculture* 6(2): 210–224. doi: 10.5455/faa.136276

1 Introduction

Tomato (*Solanum lycopersicum* L.) belongs to the family Solanaceae which prefers to grow in shady regions and flowers at night (Knapp, 2002). Tomato is the second most valuable vegetable crop in the world. Its current production is 182.3 million tons of fruits per year from a total cultivated area of 4.85 million ha (FAOSTAT, 2019). It is the world's one of the most commonly grown and consumed crops (Asero, 2013). Tomato is regarded as the most commonly cultivated and processed crop in the world (Tiwari et al., 2020). Tomato is believed to be originated in South American region which comprises parts of Chile, Bolivia,

Ecuador, Colombia, and Peru from the Andean region of modernity (Peralta and Spooner, 2007). Currently China, India, the United States, Egypt, and Turkey are the world's five top tomato producers in the world (FAOSTAT, 2013). Medicinal values of tomato has been realized since the adoption of ancient medicinal procedures such as Ayurveda, Homeopathy, Unani, Chinese and Tibetan medicines (Tiwari et al., 2020). Tomato is a phytomedicinal plant which consists of various categories of vitamins, carotenoids, phenolic compounds [flavonoids and hydroxycinnamic acid derivatives, minerals (K, Ca, Mn, Zn, and Cu) and lectins] and phenolic acid (caffeic acid, ferulic acid,

and p-coumaric acid).

Tomato is rich in bioactive compounds (L-ascorbic acid, lycopene, and β -carotene). Due to presence of antioxidants such as carotenoid, ascorbic acids and other different bioactive compounds, tomato exhibits a broad spectrum and array of physiological properties including anti-inflammatory, cardio-protective, antioxidant anti-allergenic, antimicrobial, vasodilatory and antithrombotic properties (Raiola et al., 2014). Carotenoid-rich tomatoes are one of the major sources of lycopene in the human diet (Viuda-Martos et al., 2014). The nutritional benefit of tomato is strengthened by carotenoids and polyphenolic compounds, as well as their functional and sensory attributes such as taste, flavor, and texture (Raiola et al., 2014; Tohge and Fernie, 2015a; Marti et al., 2016). Because of increasing economic and nutritional interests and widespread development as a model research plant, tomato remains a leading plant in agricultural research worldwide (Kimura and Sinha, 2008).

Tomato fruits are a significant source of substances with well-known health-promoting properties, like vitamins, nutrients, and antioxidants, especially ones of many other plant species that contribute to our diet (Frusciante et al., 2007). Tomatoes produce various therapeutic compounds and are readily included in a healthy diet as a nutritious component (Marti et al., 2016). Their specific health-promoting substances, such as antioxidants, carotenoids, and phenol compounds, clarify the dietary benefit of tomatoes (Raiola et al., 2014; Liu et al., 2016; Marti et al., 2016; Li et al., 2019). Antioxidant inhibits the production of free radicals formed in our body as a result of biological oxidation (Modi, 2019). Indeed, a decrease in the incidence of inflammatory factors, cancer, and chronic non-communicable diseases (CNCD) including cardiovascular disorders (CVD) such as hypertension, diabetes, coronary heart problems, and obesity has been correlated with a tomato fruit intake (Canene-Adams et al., 2005). Consumers have become increasingly acquainted with the safety advantages of diets and their position in avoiding a variety of medical illnesses and dysfunctions over the last decade (Pem and Jeewon, 2015). While a significant number of functional foods have been developed to meet such criteria, it should be noted that the use of 'conventional foods' including fruits and vegetables in this regard is more successful (Viuda-Martos et al., 2014).

Tomato has unique characteristics as owing to its diploid ($2n = 2x = 24$), fairly compact and subsequently sequenced genome and its substantial genetic and genomic resources, it is the first vegetables in cultivation worldwide, and a model plant species (Ranjan et al., 2012). A sequencing process is underway for the whole tomato genome, which is an abundant genomic resource and for this crop all genetic, physical and molecular maps are achievable (Consortium, 2012; Suresh et al., 2014; Zhou et al., 2019). Many

factors like water scarcity, soil salinization as well as other abiotic stresses, pose a challenge to tomato production (Fahad et al., 2017; Gharbi et al., 2017; Zhou et al., 2019). This relationship will affect plant growth and yield depending on nutrient availability (Pandey et al., 2020). The application of nitrogen, phosphorus, potassium, and micronutrients such as Zn and S containing fertilizers is intimately correlated to plant development, growth, and production (Shrestha et al., 2020a). One important aspect that is of direct significance to crop production is the size of the field or plot, providing crops with the required amount of nutrients at the right time, soil fertility management, and nutrient distribution (KC et al., 2020). Different cultivation practices influence the production of tomato fruits and the biosynthesis of the metabolites (Diouf et al., 2018). Tomatoes have been the paradigm for the study of fleshy fruit production as well as their economic and nutritional importance (Karlova et al., 2014; Kim et al., 2018; Li et al., 2019). Consumers use tomatoes in processed products such as soups, juices, and sauces in addition to consuming fresh fruits (Krauss et al., 2006; Li et al., 2018).

The objective of this review was to assess the bioactive compounds along with their pharmacological actions found in tomato. This review would be useful to nutritionists, agriculturist and health workers.

2 Bio-active components and their Pharmacological actions

Bioactive compounds may naturally be found in various foods. Most of the bioactive compounds have antioxidant, anticarcinogenic, anti-inflammatory, and antimicrobial properties. Therefore, many epidemiologic studies report that some of them also have protective effects on cardiovascular diseases Hamza-lıoğlu and Gokmen (2016). The complex matrix of compounds present in tomato pose many health benefits for the human beings. The different class of bioactive compounds and their health benefits is given in Table 1. The chemical structure of some bioactive compounds of tomato are given in Fig. 1.

2.1 Lycopene

Lycopene is an acyclic β -carotene isomer which is one of the carotenoids and lipid-soluble anti-oxidants that is spontaneously synthesized by different plants, microorganisms, and other algae and fungi but not in mammals (Paiva and Russell, 1999). Chemical structure of lycopene consists of 11 conjugated and 2 non-conjugated, double bonds, which makes it a strongly unsaturated, hydrocarbon (Nguyen and Schwartz, 1999). As a polyunsaturated molecule lycopene consists of a total of 13 double bonds which can be

present in trans and cis- configurations (Hernandez-Marin et al., 2013). Since it is a polyene; it undergoes light, heat, and chemical-induced cis-trans isomerization (Zechmeister et al., 1941). Lycopene from natural plant sources exists predominantly in an all-trans configuration, the most thermodynamically stable form (Nguyen and Schwartz, 1999; Zechmeister et al., 1941) (Fig. 1). Lycopene is observed in human plasma as an isomeric structure of 50% as cis isomers and is twice as strong as β -carotene with a single-oxygen-quenching potential and 10-times stronger than α -tocopherol (Clinton et al., 1996; DiMascio et al., 1989). Lycopene content has been widely studied using several techniques such as FT-IR, Raman spectroscopy and so on (Baranska et al., 2006). Recent studies utilize the combined power of confocal and atomic force microscopy (AFM) to study cellular and subcellular feature in plant and animal cells. Confocal microscopy technique has shown that chloroplast is converted into chromoplasts accumulating large amount of lycopene (Andrea et al., 2014). Selected parts could be used to study the feature of tomato fruit by using AFM (Chatterjee et al., 2012).

Lycopene has important antioxidative function which makes it a free radical scavenger of reactive oxygen species (ROS), which is induced by partial oxygen reduction (Friedman, 2013). In addition, reactive species of nitrogen (RNS) may be generated. Free radicals and other non-radicals also recognized as oxidants (Halliwell and Cross, 1994) are classified by ROS and RNS. Lycopene can be present in fresh, all-trans (79–91%) and cis (9–21%) isomers (Shi et al., 1999; Boileau et al., 2002a; Abdel-Fattah and Al-Amri, 2012) of red-ripe tomatoes. The primary nutrients N, P, K, for plants, are nutrients that aid in constructing and disseminating organ yield and quality, physiological qualities, and component synthesis (Shrestha et al., 2020b). With an increasing level of potassium, the lycopene content in the nutrient solution rise linearly (Serio et al., 2007). Tomatoes grown in the field seem to have higher lycopene concentrations between 5.2 mg/100 g fresh weight (FW) and 10.8 mg/100 g FW (Ansari and Gupta, 2004) than tomatoes grown in a greenhouse. Lycopene converts green tomato to red, whereas thermal therapies such as illumination, acids, oxygen, and digestion can contribute to a more bio-active cis-form transition (Boileau et al., 2002b).

2.1.1 Role of lycopene in cancer

It has been reported from various studies that a tomato rich diet has protective effects against number of chronic diseases by removing or reducing oxidative stress. The dietary intake of lycopene supplement in one week has been reported to lower the endogenous rates of lipid oxidation, protein oxidation, lipoprotein oxidation, and DNA (Agarwal and Rao, 1998; Rao and Agarwal, 1998). The intake of 10 mg ly-

copene/day has been reported to reduce metastatic prostate cancer from the stage PSA (Specific Antigen Prostate), tumor type, bone pain, and urinary tract symptoms (Ansari and Gupta, 2004) interfering with activation of the receptor component of development and initiation of the cell cycle (Amir et al., 1999).

Moreover, lycopene can also suppress certain forms of cancer (endometrial, lung, breast, colorectal, oral, and pancreatic) (Gonzales-Vallinas et al., 2013). Furthermore, lycopene is not effective enough as a treatment for prostate cancer, according to some reports, since substantial quantities (above 1 mmol/L) are required for significant human reaction (Ilic et al., 2011, 2013; Sporn and Liby, 2013). Epidemiologic studies have suggested that 6 mg per day is beneficial for prostate cancer prevention. Higher lycopene concentrations of 35 mg to 75 mg per day could be appropriate for reducing risk of diseases such as cancer and cardiovascular disorders (Heath et al., 2006). Tomato products intake anti-inflammatory properties outweigh the lycopene in a single compound (Hazewindus et al., 2012; Riso et al., 2006).

Several reports have demonstrated a substantial reduction in the incidence of cancer by increasing the consumption and serum rates of lycopene (Kucuk et al., 2001; Rao and Rao, 2004; Rao et al., 2006). Among newly diagnosed cancer patients who were obtaining 15 mg of lycopene 3 weeks per day, before drastic prostatectomy was confirmed to have lycopene lowered their PSA rates and prostate cancer growth (Kucuk et al., 2001; Kucuk and Wood, 2002). A reduced chance of prostate cancer from 30–40% with regular intake with products high in lycopene (Giovannucci et al., 2002).

Additional research found a substantial rise in serum and prostate levels of lycopene (Bowen et al., 2002) by consuming tomato sauce 30 mg lycopene a day prior to prostatectomy in males diagnosed with prostate cancer (Bowen et al., 2002). Pilot trials in patients with prostate cancer have demonstrated a tumor development and invasively that is possibly decreased by the routine intake of lycopene produced from tomato sauce or tomato extract, both by connexin 43 (Cx43) (tumor suppressor protein) control (Kucuk et al., 2002). *Solanum sisymbriifolium* (Solanaceae) one of the invasive alien species of tomato's phytochemical compounds, bioactive compounds as lycopene and antioxidant activities helps to cure hypotension activity, cardio-vascular disease and anticonvulsant activity (Gupta et al., 2014). Heber and Lu (2002) showed, from preclinical and clinical studies, that a gene connexin 43 whose expression has been uplifted and controlled through lycopene, allowed for direct intercellular gap junctional communication (GJC). Nkondjock et al. (2005) have reported that lycopene reduces the prevalence of pancreatic cancer in the diet of tomatoes with a large content of lycopene as well as the intake of tomato products.

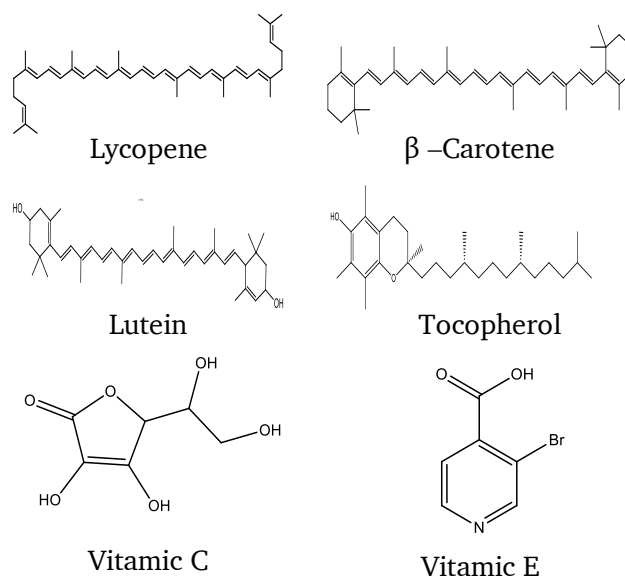


Figure 1. Chemical structure of some bioactive compounds of tomato. Redrawn from [Nguyen and Schwartz \(1999\)](#) and [Zechmeister et al. \(1941\)](#).

2.1.2 Role of lycopene in cardiovascular disease

Lycopene protects against myocardial infarction and stroke ([Arab and Steck, 2000](#)). In addition to the antioxidant effect, the protective effect of lycopene was thought to be triggered by some other process. The same happens in the case of early atherosclerosis and enhanced intima thickness media in the ordinary carotid artery wall (CCA-IMT), as stated by [Rissanen et al. \(2002\)](#). In an study it was reported that the consumption of tomato sauce, tomato juice or lycopene oleo-resin capsules, and thereby shields LDL from *in vitro* oxidations; substantially reduce rates of the oxidized LDL/ lipid peroxidation ([Safari, 2007](#)).

2.1.3 Other roles of lycopene

The role of lycopene in male fertility is being investigated by researchers. Lycopene protects sperm from the oxidative damage. Studies show that people with antibody influenced infertility have less serum lycopene than their fertile tests ([Palan and Naz, 1996](#)). Lycopene has been demonstrated to avoid cataract genesis due to its antioxidant ability ([Gupta et al., 2009](#)). In earlier research, lycopene prevented the sugar mediated diabetic cataract ([Mohanty et al., 2002](#)). Further study may explore the role of lycopene in various human conditions such as diabetes, rheumatoid arthritis, periodontal diseases, and inflammatory disorders ([Rao et al., 2006](#)). Modern pharmaceutical applications; nutraceutical and cosmeceutical products are opening up the antioxidant potency of lycopene and can at an initial stage inhibit the development or progression of many human diseases, and improve life quality ([Stahl, 2006](#)). The treatment of lycopene by 3-nitropropionic (acid-induced) rats

significantly improves the memory of the system and restores the functioning of the glutathione system ([Kumar and Kumar, 2009](#)). [Akbaraly et al. \(2007\)](#) also suggested that low levels of lycopene plasma may lead to cognitive impairment.

2.2 Carotenoids

Carotenoids contribute to the photosynthetic machinery and protect them from photo-damage ([Rao and Rao, 2007](#)). Over 600 identified carotenoids in nature, of which around 40 are common in foods included in human diets ([Gerster, 1997](#)). Carotenoids induce changes in the expression of several cell proliferation and signaling pathways proteins. Cyclin D1 is an oncogene that is overexpressed in many breast cancer cell lines. Lycopene is associated with cyclin D1 protein reduction. Lycopene also can increase the expression of many proteins that are associated with differentiation, such as cell surface antigen (CD14), explosive oxygen, and receptors of the chemo-tactic peptide ([Sharoni et al., 2004](#)). Dietary supplementation carotenoids can function as moderate hypocholesterolemic agents, resulting in a reduction of the rate limitation enzyme in cholesterol synthesis (HMG-CoA) on macrophage 3-hydroxy-3-methyl glutaryl coenzyme A ([Heber and Lu, 2002](#)).

2.2.1 β -Carotene

Carotenoids, which including β -carotene is an essential antioxidant protective factors in living cells against lipid peroxidation ([Agarwal et al., 2005](#)). Erythema development has been decreased significantly if β -carotene is used for 12 weeks in human skin or in combination with alpha-tocopherol or alone

dietary intervention (Stahl and Sies, 2003). American Institute for Cancer Research (AICR Food, 2016) concluded that the beneficial effects on prostatic cancer, carotenoid-containing foods are protected against mouth, pharyngeal, and larynx cancers, as well as lung cancer and, are particularly oesophageal cancer are protected by lycopene (β -carotene). The increased risk of CHF (congestive cardiac failure) and cardiac death in men could be associated with low serum β -carotene concentrations (Karppi et al., 2013). Data from epidemiological research has demonstrated that higher beta carotene intake can decrease the risk of cancer and prevent various chronic disorders, including cancer, cardiovascular, neurological, and ocular disorder (Khachik et al., 1996; Wood, 2001; Lavecchia, 1998; Giovannucci, 1999). Dietary tomato paste protects against ultraviolet light-induced erythema in humans. Tomato paste is applied daily on dorsal skin over 10 weeks protects against UV radiation (Stahl et al., 2001).

2.2.2 Lutein

Lutein is a yellow carotenoid that is synthesized in chloroplasts and chromoplasts. It is found in large quantities in the leaves (DellaPenna and Pogson, 2006; Giorio et al., 2013). Improved interest in lutein and zeaxanthin was due to its significant role for the protection of eye disease (Granado et al., 2003). Age-related macular degeneration (ARMD) is the leading cause of vision loss in aging Western societies. It is a disease involving genetic, neurological, nutritional, and environmental influences, the intake of lutein and zeaxanthin was found better for curing this disease (Richer et al., 2004; SanGiovanni et al., 2007). Moreover, lutein also performs various essential biological roles, such as cancer and the prevention of cardiovascular diseases and oxidant-induced cell damage defense (Arnal et al., 2010; Lakshminarayana et al., 2010; Nakagawa et al., 2009). Nevertheless, the connection between lutein consumption and normal vision maintenance has not yet been demonstrated clearly (European Food Safety Authority, 2012).

2.2.3 Medicinal value of carotenoids

Several studies have reported the health benefits of carotenoids in connection with their antioxidant properties, such as stimulation of the immune system and antitumors (Gonzales et al., 2011; Ciccone et al., 2013; Maiani et al., 2009). The most important nutritional contribution of this fruit is carotenoid intake from tomatoes and therefore carotenoid content has the highest weight within the Antioxidant Nutritional Quality Index (Frusciante et al., 2007). The main dietary form of provitamin A is plant carotenoids, with β -carotene. The absorption of carotenoids is confined to the small intestine or duodenum, which is essential

for vitamin E (alpha-tocopherol) absorption (van Bennekum et al., 2005). The nutritional value of tomatoes is enhanced by carotenoids and polyphenolic compounds. These compounds also improve the quality features and sensory attributes, namely taste, aroma, and appearance (Tohge and Fernie, 2015a).

2.3 Vitamins

Tomato contains natural antioxidants, such as Vitamin C and Vitamin E (Agarwal and Rao, 2000; Marti et al., 2016) and significant amounts of metabolites including sucrose, hexoses, citrate, malate, and ascorbic acid (Li et al., 2019). Tomato is rich in minerals, vitamins (Vitamin A and vitamin C), and lycopene. Tomato is extremely waterborne and has low calories (Wilcox et al., 2003). Vitamin C is an oxidant that eliminates the cancer risk, arteriosclerosis and heart disease (Sablani et al., 2006). Tocopherol is the richest in tomato plants and helps maintain plant photosynthesis at an optimum level under high stress. Frusciante et al. (2007) found that in tomatoes the levels of vitamin E ranged from 0.17 to 0.62 mg/100 g Supplemental vitamin E was associated with a decreased risk of prostate cancer among smokers and supplemental beta-carotene was associated with a decreased risk of prostate cancer among men with low baseline plasma beta-carotene levels (Kirsh et al., 2006). The study evaluating the impact of including tomato extract in the treatment schedule showed an important link between systolic and antioxidant activity rates and in the treatment of moderate hypertension with uncontrolled blood pressure levels (Paran et al., 2009).

Tomato fruit contains an increased and full value of ascorbic acid when ripened and then declines (Malewski and Markakis, 1971). Yahia et al. (2001) reported that Ascorbic acid in tomato fruit increased slowly reaching a maximum of 94.9 mg/100 g at 74 days and then declined slowly. The decrease in ascorbic acid coincided with the initiation of ripening, as indicated by color change, and with an increase in the activity of ascorbate oxidase. The insufficient ascorbic acid intake leads to scurvy, a disease with dry skin, open skin sores, weariness, wound-related impairment, and depression (Olson, 1999; Naidu, 2003). Some studies have shown that ascorbic acid can prevent cancer by neutralizing free radicals before it can destroy DNA and cause tumor growth or help the body to tumor destruction in early phases acting as a prooxidant (Block, 1991).

Total cholesterol and CRP (C-reactive protein) levels have decreased for 2 weeks due to the consumption of tomato sage (500 mL), a marker of inflammations (Jacob et al., 2008). Folate metabolism is part of many andrological and gynecological physiological mechanisms (Forges et al., 2007). Foliates play a particular role in various transmission reactions of one carbon, including purine and pyrimidine biosynthe-

Table 1. Different class of chemical compounds found in tomato and their health effect

Class	Compound	Main effects	References
Carotenoids	Lycopene	Cancer inhibition (colorectal, prostate, breast, endometrial, oral, lung, and pancreatic)	Gonzales-Vallinas et al. (2013); Ansari and Gupta (2004)
	β-Carotene	Photooxidant damage prevention	Stahl and Sies (2003)
		Atherosclerosis inhibition and myocardial infarction prevention	Karppi et al. (2013)
	Lutein	Eye health protection and symptom improvement in ARMD	Richer et al. (2004); San-Giovanni et al. (2007)
Vitamins	Vitamin E	Improved endogenous damage and repair resistance to DNA	Herrero-Barbudo et al. (2013)
		Inhibition of cardiovascular diseases and lipid peroxidation	Hazewindus et al. (2012); Abushita et al. (2000)
	Vitamin C	Decreasing risks of advanced prostate cancer and type II diabetes	Kirsh et al. (2006); Montonen et al. (2004)
		LDL oxidation inhibition, and monocyte adhesion	Rodriguez et al. (2005); Li and Schellhorn (2007)
	Folates	Total cholesterol and CRP decrease	Jacob et al. (2008)
		Monitoring homocysteine metabolism	Solini et al. (2006)
		Lowering the risk of neural tube defects	Wals et al. (2007)
Phenolics	Flavonoids	Anti-inflammatory intestinal activity	Martin et al. (2006)
		TNF- alpha inhibition -mediated inflammation	Gonzales et al. (2011)
	Phenolic acids	DNA oxidation protection and antitumor activity against carcinogenesis in the colon	Lodovici et al. (2001); Prasad et al. (2011)
	Tannins	Adipogenesis inhibitors	Seabra et al. (2006)
		Antibacterial, antiviral, cardiovascular, anti-carcinogenic action	Koleckar et al. (2008)

sis, metabolism of amino acids, methylation of nucleic acid proteins, and lipids (Lucock, 2000). Folates are therefore essential for fetal growth (Wagner, 1995). The addition of folic acid (200–400 mg/day) is recommended for women who are pregnant (FNBNC, 1970). Nishiimi et al. (2011) reported that tannins can enhance glucose absorption and inhibit adipogenesis, which acts like possible medicines for the treatment of noninsulin-dependent diabetes mellitus (Seabra et al., 2006). Koleckar et al. (2008) reported that tannins play a role in the pathways of anti-bacterial, antiviral, anti-cancerous and avoidance of cardiovascular activity in addition to anti-inflammatory effects.

2.4 Phenolic compounds

Common sources of bioactive natural substances such as secondary metabolites and antioxidants are plants (Ghasemzadeh and Ghasemzadeh, 2011). Polyphenols are secondary plant metabolites and are commonly used to protect the skin from UV radiation or

pathogens aggressions (Kumar and Pandey, 2013). Plants contain large quantities of bioactive phyto-components, for example, phenolics, flavonoids, tannins (Parajuli et al., 2012). Phenolic acids, flavones, including hydroxycinnamic acid lignans, stilbenes, coumarins, and tannins, are typically found in food-stuffs as the most common phenolic acids (Harborne and Williams, 2000). Phenolic compounds in tomatoes have been considered accountable in addition to their lycopene content for antioxidant activity (Takeoka et al., 2001). Tomato contains up to 200 mg gallic acid equivalents for each 100 g (as dried weight) of total phenolic content (Kahkonen et al., 1999). Tomato polyphenols, mainly phenolic acids, are present in an insoluble-bound form, otherwise present in free soluble form. In tomatoes flavonols has a high antioxidant activity (Shahidi et al., 1992). The key factors affecting the quantity and composition of phenolic compounds present in food are genotype, storage conditions, extraction process and environmental conditions (Luthria et al., 2006).

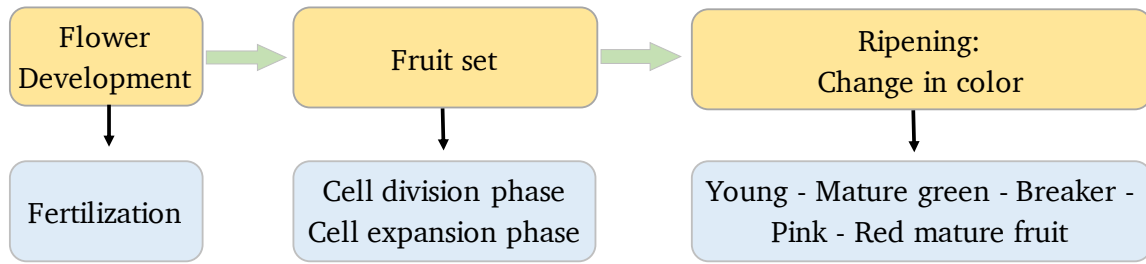


Figure 2. Main stages of tomato fruit development, ripening and maturation. Redrawn from Gillaspay et al. (1993).

3 Pharmacological properties of tomato

Recently tomato has gained recognition for the prevention of some human diseases (Table 1). This is because of carotenoids, especially lycopene appears to be an active substance in cancer prevention, cardiovascular risk, and slowed down cellular aging (Gerster, 1997; DiCesare et al., 2012; Abdel-Fattah and Al-Amri, 2012). Tomato is health-effective by decreasing the risk of cancer and cardiovascular diseases due to its high lycopene and β -carotenes, serving as antioxidants and free radical scavenger (Giovannucci, 1999). On the other hand, tomato consumption can cause allergic reactions attributed to the prevalence of various allergenic proteins (Martin-Pedraza et al., 2016). High intakes of tomato products in the diet can reduce LDL cholesterol levels and increase LDL oxidation resistance (Silaste et al., 2007). During the meal, tomato intake decreased oxidative stress caused by postprandial lipemia and related inflammatory responses (Burton-Freeman et al., 2012). Tomatoes have also played a significant role to play in maintaining DNA stability. Daily intake of tomato drinking known as Lyc-O-Mato reduces DNA damage to lymphocytes under oxidative stress considerably by approximately 42% (Porrini et al., 2005). A substantial decrease in mortality (48%) and a decreased risk of death from diarrhea have been related to the consumption of tomatoes 2-3 days compared to zero days (Fawzi et al., 2000).

4 Metabolic changes in totmato

Dramatic metabolic changes occur during tomato fruit development (Carrari and Fernie, 2006). Tomato is a climateric fruit, it is subjected to a rise in respiration and ethylene at the beginning of maturation (Li et al., 2019). As maturation progress (Fig. 2), tomato fruits move through the simultaneous sorting of the chloroplast through the chromoplasts and the domination of carotenoids and lycopene in ripe fruit cells from a partly photosynthetic to actual heterotrophic tissue (Carrari and Fernie, 2006). Ripening stimu-

lates pathways that typically affect the number of pigments, sugars, acids, and flavors, making the fruit more enticing and at the same time facilitating softening and deterioration of the tissue, which promotes seed release (Matas et al., 2009). The quality of tomato fruits and the biosynthetic pathway of metabolites are influenced by plant growing conditions.

4.1 Primary metabolism

The growth of fleshy tomato fruits takes place in three different phases. Tomatoes undergo a transition phase from a partly photosynthetic to a total heterotrophic metabolism during this evolution. Including young, mature green, breaker, pinkish and red mature fruit, are called typical morpho-physiological measures. While fruit ripening is an important step in determining fruit quality and nutrient values, recent work has shown that early fruit development also has key functions for quality acquisitions, including the accumulation of organic acids and sugars (Carrari and Fernie, 2006; Beauvoit et al., 2014; Biais et al., 2014; Bauchet et al., 2017).

4.2 Secondary metabolism

The onset and progression of ripening in tomato is typically linked to changes in the external color of pericarp that reflects the accumulation of carotenoids and flavonoid pigments (Shinozaki et al., 2018). The characteristic red tomato color is a result of the accumulation of the carotenoid lycopene in both the fruit skin as well as pulp (Seymour et al., 2013; Borghesi et al., 2016; Ambrosio et al., 2018). Carotenoids increase by 10-to 14-fold during tomato ripening, primarily because of the accumulation of lycopene. Fraser et al. (1994) found that as the fruit matures that increase lycopene (Tamasi et al., 2019). During tomato fruit maturation light signaling and plant hormones, especially ethylene and lesions, have been recognized as important regulators of carotenoid biosynthesis (Cruz et al., 2018). Semi-polar metabolites such as flavonoids, phenolic acids, and alkaloids also accumulate in tomatoes, which are important compounds to promote public health (Bovy et al., 2007; Tohge

and Fernie, 2015b; Ballester et al., 2016; Tohge et al., 2017; Tamasi et al., 2019; Wang et al., 2019). The fruit taste and aroma are caused by volatile metabolites biosynthesized during tomato ripening (Carrari and Fernie, 2006; Ballester et al., 2016; Shinozaki et al., 2018). Over 400 volatiles were contained in tomatoes, but a smaller range of 15 to 20 was produced in sufficient quantities to influence humans' perception (Baldwin et al., 2000; Mathieu et al., 2009; Zanor et al., 2009).

5 Conclusion

Tomatoes has been studied extensively for fresh fruit production and active compounds regarding its nutritional, health and economic benefits. Tomatoes are consumed fresh or in the form of processed products. Tomato is the second most consumed vegetable worldwide, thus being an important source of nourishment for the world's population. It is rich in bioactive compounds such as lycopene, carotenoids, β -carotene, lutein and vitamins, which contribute to health-promoting effects. This study highlights the antioxidant properties, metabolism, nutritional values with health benefits of tomato. Tomato is enriched in antioxidants with anti-carcinogenic properties. Tomato consumption tends to improve the vision, and also helps in tumor and skin diseases. In the years to come research on tomatoes should be centered in improving the quality and taste as well as extraction and commercialization of the active compounds that has health and nutritional benefits.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- Abdel-Fattah GM, Al-Amri SM. 2012. Induced systemic resistance in tomato plants against *Fusarium oxysporium* F. sp. lycopersici by different kinds of compost. *Biotechnology* 11:12454–12463.
- Abushita A, Daood HG, Biacs PA. 2000. Change in carotenoids and antioxidant vitamins in tomato as a function of varietal and technological factors. *Journal of Agricultural and Food Chemistry* 48:2075–2081.
- Agarwal A, Prahakaran SA, Said TM. 2005. Prevention of an oxidative stress injury to sperm. *Journal of Andrology* 26:653–660. doi: 10.2164/jandrol.05016.
- Agarwal S, Rao AV. 1998. Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. *Lipids* 33:981–1056.
- Agarwal S, Rao AV. 2000. Tomato lycopene and its role in human health and chronic diseases. *CMAJ* 163:739–744.
- AICR Food. 2016. Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective. Accessed from http://www.aicr.org/assets/docs/pdf/reports/Second_Expert_Report.pdf on 01 May 2016.
- Akbaraly NT, Faure H, Gourlet V, Favier A, Berr C. 2007. Plasma carotenoid levels and cognitive performance in an elderly population: Results of the EVA Study. *The Journals of Gerontology Series A Biological Sciences and Medical Sciences* 62:308–316.
- Ambrosio D, Stigliani C, Giorio AL. 2018. CRISPR/Cas9 editing of carotenoid genes in tomato. *Transgenic Research* 27:367–378. doi: 10.1007/s11248-018-0079-9.
- Amir H, Karas M, Giat J. 1999. Lycopene and 1, 25-dihydroxyvitamin D3 cooperate in the inhibition of cell cycle progression and induction of differentiation in HL-60 leukemic cells. *Nutrition and Cancer* 33:44–49.
- Andrea D, Amenos LM, Rodriguez-Concepcion M. 2014. Confocal laser scanning microscopy detection of chlorophylls and carotenoids in chloroplasts and chromoplasts of tomato fruit. In: *Plant Isoprenoids*. Humana Press, New York, USA. doi: 10.1007/978-1-4939-0606-2_16.
- Ansari MS, Gupta NP. 2004. Lycopene: a novel drug therapy in hormone refractory metastatic prostate cancer. *Urologic Oncology* 22:415–420.
- Arab L, Steck S. 2000. Lycopene and cardiovascular disease. *The American Journal of Clinical Nutrition* 71:1691–1695.
- Arnal E, Miranda M, Barcia J, Bosch-Morell F, Romero FJ. 2010. Lutein and docosahexaenoic acid prevent cortex lipid peroxidation in streptozotocin-induced diabetic rat cerebral cortex. *Neuroscience* 166:271–278.
- Asero R. 2013. Tomato allergy: clinical features and usefulness of current routinely available diagnostic methods. *The Journal of Investigational Allergology and Clinical Immunology* 23:37–42.
- Baldwin EA, Scott JW, Shewmaker CK, Schuch W. 2000. Flavor trivia and tomato aroma: biochemistry and possible mechanisms for control of important aroma components. *HortScience* 35:1013–1022. doi: 10.21273/hortsci.35.6.1013.

- Ballester AR, Tikunov Y, Molthoff J, Grandillo S, Viquez-Zamora M. 2016. Identification of loci affecting accumulation of secondary metabolites in tomato fruit of a *Solanum lycopersicum* × *Solanum chmielewskii* introgression line population. *Frontiers in Plant Science* 7:1428. doi: [10.3389/fpls.2016.01428](https://doi.org/10.3389/fpls.2016.01428).
- Baranska M, Schutze W, Schulz H. 2006. Determination of lycopene and β -carotene content in tomato fruits and related products: comparison of FT-Raman, ATR-IR, and NIR spectroscopy. *Analytical Chemistry* 78:8456–8461. doi: [10.1021/ac061220j](https://doi.org/10.1021/ac061220j).
- Bauchet G, Grenier S, Samson N, Segura V, Kende A, Beekwilder J. 2017. Identification of major loci and genomic regions controlling acid and volatile content in tomato fruit: implications for flavor improvement. *New Phytologist* 215:624–641. doi: [10.1111/nph.14615](https://doi.org/10.1111/nph.14615).
- Beauvoit BP, Colombié S, Monier A, Andrieu MH, Biais B, Bénard C, Chéniclet C, Dieuaide-Noubhani M, Nazaret C, Mazat JP, et al. 2014. Model-assisted analysis of sugar metabolism throughout tomato fruit development reveals enzyme and carrier properties in relation to vacuole expansion. *The Plant Cell* 26:3224–3242. doi: [10.1105/tpc.114.127761](https://doi.org/10.1105/tpc.114.127761).
- Biais B, Benard C, Beauvoit B, Colombie S, Prodhomme D, Menard G. 2014. Remarkable reproducibility of enzyme activity profiles in tomato fruits grown under contrasting environments provides a roadmap for studies of fruit metabolism. *Plant Physiology* 164:1204–1221. doi: [10.1104/pp.113.231241](https://doi.org/10.1104/pp.113.231241).
- Block G. 1991. Vitamin C and cancer prevention: the epidemiological evidence. *American Journal of Clinical Nutrition* 53:270–282. doi: [10.1093/ajcn/53.1.270S](https://doi.org/10.1093/ajcn/53.1.270S).
- Boileau TWM, Boileau AC, Erdman JW. 2002a. Bioavailability of all-trans and cis-isomers of lycopene. *Experimental Biology and Medicine* 227:914–919.
- Boileau TWM, Boileau AC, Erdman JW. 2002b. Bioavailability of all-trans and cis-isomers of lycopene. *Experimental Biology and Medicine* 227:914–919.
- Borghesi E, Ferrante A, Gordillo B, Rodríguez-Pulido F, Cocetta G, Trivellini A. 2016. Comparative physiology during ripening in tomato rich-anthocyanins fruits. *Plant Growth Regulators* 80:207–214. doi: [10.1007/s10725-016-0158-y](https://doi.org/10.1007/s10725-016-0158-y).
- Bovy A, Schijlen E, Hall RD. 2007. Metabolic engineering of flavonoids in tomato (*Solanum lycopersicum*): the potential for metabolomics. *Metabolomics* 3:399–412. doi: [10.1007/s11306-007-0074-2](https://doi.org/10.1007/s11306-007-0074-2).
- Bowen P, Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, Kim HS, Christov-Tzelkov K, VanBreemen R. 2002. Tomato sauce supplementation and prostate cancer: lycopene accumulation and modulation of biomarkers of carcinogenesis. *Experimental Biology and Medicine* 227:886–893.
- Burton-Freeman B, Talbot J, Park E, Krishnankutty S, Edirisinghe I. 2012. Protective activity of processed tomato products on postprandial oxidation and inflammation: a clinical trial in healthy weight men and women. *Molecular Nutrition and Food Research* 56:622–631.
- Canene-Adams K, Campbell JK, Zaripheh S, Jeffery EH, Erdman Jr JW. 2005. The tomato as a functional food. *The Journal of nutrition* 135:1226–1230.
- Carrari F, Fernie AR. 2006. Metabolic regulation underlying tomato fruit development. *Journal of Experimental Botany* 57:1883–1897. doi: [10.1093/jxb/erj020](https://doi.org/10.1093/jxb/erj020).
- Chatterjee S, Sarkar S, Oktawiec J, Mao Z, Niitsoo O, Stark RE. 2012. Isolation and biophysical study of fruit cuticles. *Journal of Visualized Experiments* 30:e3529. doi: [10.3791/3529](https://doi.org/10.3791/3529).
- Ciccone MM, Cortese F, Gesualdo M. 2013. Dietary intake of carotenoids and their antioxidant and anti-inflammatory effects in cardiovascular care. *Mediators of Inflammation* 2013:11.
- Clinton SK, Emenhiser C, Schwartz SJ, Bostwick DG, Williams AW, Moore BJ. 1996. Cis-trans lycopene isomers, carotenoids and retinol in the human prostate. *Cancer Epidemiol Biomarkers Prevention* 5:823–33.
- Consortium TG. 2012. The tomato genome sequence provides insights into fleshy fruit evolution. *Nature* 485:635–641.
- Cruz AB, Bianchetti RE, Alves FRR, Purgatto E, Peres LEP, Rossi M. 2018. Light, ethylene and auxin signaling interaction regulates carotenoid biosynthesis during tomato fruit ripening. *Frontiers in Plant Science* 9:1370–1390. doi: [10.3389/fpls.2018.01370](https://doi.org/10.3389/fpls.2018.01370).
- DellaPenna D, Pogson BJ. 2006. Vitamin synthesis in plants: tocopherols and carotenoids. *Annual Review of Plant Biology* 57:711–738.

- DiCesare LF, Migliori C, Ferrari V, Parisi M, Campanelli G, Candido V, Perrone D. 2012. Effects of irrigation-fertilization and irrigation-mycorrhization on the alimentary and nutraceutical properties of tomatoes.
- DiMascio P, Kaiser S, Sies H. 1989. Lycopene as the most effective biological carotenoid singlet oxygen quencher. *Arch Biochem Biophys* 2:532–577.
- Diouf IA, Derivot L, Bitton F, Pascual L, Causse M. 2018. Water deficit and salinity stress reveal many specific qtl for plant growth and fruit quality traits in tomato. *Frontiers in Plant Science* 9:279–301. doi: 10.3389/fpls.2018.00279.
- European Food Safety Authority. 2012. Scientific opinion on the substantiation of health claims related to lutein and maintenance of normal vision (ID, 1603, 1604, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *Te EFSA Journal* 10:2716,.
- Fahad S, Bajwa AA, Nazir U, Anjum SA, Farooq A, Zohaib A. 2017. Crop production under drought and heat stress: plant responses and management options. *Frontiers in Plant Science* 8:1147–1201. doi: 10.3389/fpls.2017.01147.
- FAOSTAT. 2013. FAOSTAT Statistical Database. Food and Agriculture Organization of the United Nations, Rome, Italy. Available at <http://www.fao.org/faostat/en/#data/QC> on 2 October 2017.
- FAOSTAT. 2019. FAOSTAT Statistical Database. Food and Agriculture Organization of the United Nations, Rome, Italy. Available at <http://www.fao.org/faostat/en/#home> on 15 April 2019.
- Fawzi W, Herrera MG, Nestel P. 2000. Tomato intake in relation to mortality and morbidity among sudanese children. *The Journal of Nutrition* 130:2537–2542.
- FNBNC. 1970. Maternal Nutrition and the Course of Pregnancy. Food and Nutrition Board and National Research Council (FNBNC), National Academy of Sciences, Washington, DC, USA.
- Forges T, Monnier-Barbarino P, Alberto JM, Gueant-Rodriguez RM, Daval JL, Gueant JL. 2007. Impact of folate and homocysteine metabolism on human reproductive health. *Human Reproduction Update* 13:225–238.
- Fraser PD, Truesdale MR, Bird CR, Schuch W, Bramley PM. 1994. Carotenoid biosynthesis during tomato fruit development (evidence for tissue-specific gene expression). *Plant Physiology* 105:405–413. doi: 10.1104/pp.105.1.405.
- Friedman M. 2013. Anticarcinogenic, cardio protective, and other health benefits of tomato compounds lycopene, beta-tomatine, and tomatidine in pure form and in fresh and processed tomatoes. *Journal of Agricultural and Food Chemistry* 61:9534–9550.
- Frusciant L, Carli P, Ercolano MR. 2007. Antioxidant nutritional quality of tomato. *Molecular Nutrition and Food Research* 51:609–617.
- Gerster H. 1997. The potential role of lycopene for human health. *Journal of the American College of Nutrition* 16:109–126.
- Gharbi E, JP M, H B, G L, B V, M Q. 2017. Inhibition of ethylene synthesis reduces salt-tolerance in tomato wild relative species *Solanum chilense*. *Journal of Plant Physiology* 210:24–37. doi: 10.1016/j.jplph.2016.12.001.
- Ghasemzadeh A, Ghasemzadeh N. 2011. Flavonoids and phenolic acids: Role and biochemical activity in plants and human. *Journal of Medicinal Plants Research* 5:6697–6703.
- Gillaspy G, Ben-David H, Gruissem W. 1993. Fruits: a developmental perspective. *The Plant Cell* 5:1439–1451. doi: 10.1105/tpc.5.10.1439.
- Giorio G, Yildirim A, Stigliani AL, Ambrosio CD. 2013. Elevation of lutein content in tomato: a biochemical tug-of-war between lycopene cyclases. *Metabolic Engineering* 20:167–176.
- Giovannucci E. 1999. Tomatoes, tomato-based products, lycopene, and cancer: a review of the epidemiologic literature. *Journal of the National Cancer Institute* 91:317–331.
- Giovannucci E, Rimm E, Liu Y, Stamfer M, Willet WA. 2002. Prospective study of tomato products, lycopene and prostate cancer risk. *Journal of the National Cancer Institute* 94:391–398.
- Gonzales R, Ballester I, Lopez-Posadas R. 2011. Effects of favonoids and other polyphenols on inflammation. *Critical Reviews in Food Science and Nutrition* 51:331–362.
- Gonzales-Vallinas M, Gonzales-Catej M, Rodriguez-Casado A, deMolinaA R. 2013. Dietary phytochemicals in cancer prevention and therapy: a complementary approach with promising perspectives. *Nutrition Reviews* 71:585–599.
- Granado F, Olmedilla B, Blanco I. 2003. Nutritional and clinical relevance of lutein in human health. *British Journal of Nutrition* 90:487–502.
- Gupta SK, Trivedi D, Srivastava S, Joshi S, Halder N, Verma SD. 2009. Lycopene attenuates oxidative

- stress induced experimental cataract development: an *in-vitro* and *in-vivo* study. *Nutrition* 19:794–799.
- Gupta VK, Simlai A, Tiwari M, Bhattacharya K, Roy A. 2014. Phytochemical contents, antimicrobial and antioxidative activities of *Solanum sisymbriifolium*. *Journal of Applied Pharmaceutical Science* 4:075–080. doi: [10.7324/JAPS.2014.40315](https://doi.org/10.7324/JAPS.2014.40315).
- Halliwell B, Cross CE. 1994. Oxygen-derived species: their relation to human disease and environmental stress. *Environmental Health Perspectives* 102:5–12.
- Hamzalioglu A, Gokmen V. 2016. Interaction between Bioactive Carbonyl Compounds and Asparagine and Impact on Acrylamide. In: Gokmen V (Ed), *Acrylamide in Food: Analysis, Content and Potential Health Effects*. Elsevier. doi: [10.1016/b978-0-12-802832-2.00018-8](https://doi.org/10.1016/b978-0-12-802832-2.00018-8).
- Harborne JB, Williams CA. 2000. Advances in flavonoid research since 1992. *Phytochemistry* 55:481–504.
- Hazewindus M, Haenen GRM, Weseler AR, Bast A. 2012. The anti-inflammatory effect of lycopene complements the antioxidant action of ascorbic acid and beta-tocopherol. *Food Chemistry* 132:954–958.
- Heath E, Seren S, Sahin K, Kucuk O. 2006. The role of tomato lycopene in the treatment of prostate cancer in Tomatoes. Caledonian Science Press.
- Heber D, Lu QY. 2002. Overview of mechanisms of action of lycopene. *Experimental Biology and Medicine* 227:920–923.
- Hernandez-Marin E, Galano A, Martinez A. 2013. Cis carotenoids: colorful molecules and free radical quenchers. *The Journal of Physical Chemistry B* 117:4050–406.
- Herrero-Barbudo C, Soldevilla B, Perez-Sacrist B. 2013. Modulation of dna-induced damage and repair capacity in humans after dietary intervention with lutein-enriched fermented milk. *PLOS ONE* 8:1–6.
- Ilic D, Forbes KM, Hased C. 2011. Lycopene for the prevention of prostate cancer. *Cochrane database of systematic reviews*.
- Ilic D, Neuberger MM, Djulbegovic M, Dahm P. 2013. Screening for prostate cancer. *Cochrane Database of Systematic Reviews* 1:1–63.
- Jacob K, Periago MJ, Bohm V, Berrueto GR. 2008. Influence of lycopene and vitamin C from tomato juice on biomarkers of oxidative stress and inflammation. *British Journal of Nutrition* 99:137–146.
- Kahkonen MP, Hopia AI, Vuorela HJ, Rauha JP, Pihlaja K, Kujala TS, Heinonen M. 1999. Antioxidant activity of plant extracts containing phenolic compounds. *Journal of Agricultural and Food Chemistry* 47:3954–3962.
- Karlova R, Chapman N, David K, Angenent GC, Seymour GB. 2014. Transcriptional control of fleshy fruit development and ripening. *Journal of Experimental Botany* 65:4527–4541. doi: [10.1093/jxb/eru316](https://doi.org/10.1093/jxb/eru316).
- Karppi J, Kurl S, Makikallio K, Ronkainen TH, Laukkanen JA. 2013. Serum β -carotene concentrations and the risk of congestive heart failure in men: a population-based study. *International Journal of Cardiology* 168:1841–1846.
- KC S, Shah KK, Baidhya N, Neupane P, Pokhrel S, Upadhyay K, Shrestha J. 2020. Evaluation of seedling growth of rice (*Oryza sativa* L.) genotypes under water stress and non-stress conditions. *Archives of Agriculture and Environmental Science* 5:174–178. doi: [10.26832/24566632.2020.0502014](https://doi.org/10.26832/24566632.2020.0502014).
- Khachik F, Clevidence BA, Kramer TR, Nair P. 1996. Plant pigments. *Agricultural Research* 4-8.
- Kim JY, Kim SK, Jung J, Jeong MJ, Ryu CM. 2018. Exploring the sound-modulated delay in tomato ripening through expression analysis of coding and non-coding RNAs. *Annals of Botany* 122:1231–1244. doi: [10.1093/aob/mcy134](https://doi.org/10.1093/aob/mcy134).
- Kimura S, Sinha N. 2008. Tomato (*Solanum lycopersicum*): A model fruit-bearing crop. *Cold Spring Harbor Protocols* doi: [10.1101/pdb.emo105](https://doi.org/10.1101/pdb.emo105).
- Kirsh VA, Hayes RB, Mayne ST. 2006. Supplemental and dietary vitamin E, beta-carotene, and vitamin C intakes and prostate cancer risk. *Journal of the National Cancer Institute* 98:245–254.
- Knapp S. 2002. Tobacco to tomatoes: A phylogenetic perspective on fruit diversity in the Solanaceae. *Journal of Experimental Botany* 377:2001–2022.
- Koleckar V, Kubikova K, Rehakova Z. 2008. Condensed and hydrolysable tannins as antioxidants influencing the health. *Mini-Reviews in Medicinal Chemistry* 8:436–447.
- Krauss S, Schnitzler W, Grassmann J, Voitke M. 2006. The influence of different electrical conductivity values in a simplified recirculating soilless system on inner and outer fruit quality characteristics of tomato. *Journal of Agriculture and Food Chemistry* 54:441–448. doi: [10.1021/jf051930a](https://doi.org/10.1021/jf051930a).

- Kucuk O, Sarkar FH, Djuric Z, Sakr W, Pollak MN, Khachik F, Banerjee M, Bertram JS, Wood DP. 2002. Effects of lycopene supplementation in patients with localized prostate cancer. *Experimental Biology and Medicine* 227:881–885.
- Kucuk O, Sarkar FH, Sakr W. 2001. Phase II randomized clinic trial of lycopene supplementation before radical prostatectomy. *Cancer Epidemiol Biomarkers Prev* 10:861–868.
- Kucuk O, Wood DP. 2002. Response of hormone refractory prostate cancer to lycopene. *Journal of Urology* 4:167–651.
- Kumar P, Kumar A. 2009. Effect of lycopene and epigallocatechin-3-gallate against 3-nitropropionic acid induced cognitive dysfunction and glutathione depletion in rat: A novel nitric oxide mechanism. *Food and Chemical Toxicology* 47:2522–2530.
- Kumar S, Pandey AK. 2013. Chemistry and biological activities of flavonoids: an overview. *The Scientific World Journal* Article ID 162750:1–16. doi: [10.1155/2013/162750](https://doi.org/10.1155/2013/162750).
- Lakshminarayana R, Sathish UV, Dharmesh SM, Baskaran V. 2010. Antioxidant and cytotoxic effect of oxidized lutein in human cervical carcinoma cells. *Food and Chemical Toxicology* 48:1811–1816.
- Lavecchia C. 1998. Mediterranean epidemiological evidence on tomatoes and the prevention of digestive-tract cancers. *Proceedings of the Society for Experimental Biology and Medicine* 218:125–128.
- Li S, Chen K, Grierson D. 2019. A critical evaluation of the role of ethylene and MADS transcription factors in the network controlling fleshy fruit ripening. *New Phytologist* 221:1724–1741. doi: [10.1111/nph.15545](https://doi.org/10.1111/nph.15545).
- Li Y, Schellhorn HE. 2007. New developments and novel therapeutic perspectives for vitamin C. *Journal of Nutrition* 137:2171–2184.
- Li Y, Wang H, Zhang Y, Martin C. 2018. Can the world's favorite fruit, tomato, provide an effective biosynthetic chassis for high-value metabolites. *Plant Cell Reports* 37:1443–1450. doi: [10.1007/s00299-018-2283-8](https://doi.org/10.1007/s00299-018-2283-8).
- Liu Z, Alseekh S, Brotman Y, Zheng Y, Fei Z, Tieman DM. 2016. Identification of a *Solanum pennellii* Chromosome 4 Fruit Flavor and Nutritional Quality-Associated Metabolite QTL. *Frontiers in Plant Science* 7:1671. doi: [10.3389/fpls.2016.016717](https://doi.org/10.3389/fpls.2016.016717).
- Lodovici M, Guglielmi F, Meoni M, Dolara P. 2001. Effect of natural phenolic acids on DNA oxidation *in vitro*. *Food and Chemical Toxicology* 39:1205–1210.
- Lucock M. 2000. Folic acid: nutritional biochemistry, molecular biology, and role in disease processes. *Molecular Genetics and Metabolism* 71:121–138.
- Luthria DL, Mukhopadhyay S, Krizek DT. 2006. Content of total phenolics and phenolic acids in tomato (*Lycopersicon esculentum* Mill.) fruits as influenced by cultivar and solar UV radiation. *Journal of Food Composition and Analysis* 19:771–777.
- Maiani G, Caston MJ, Catasta G. 2009. Carotenoids: actual knowledge on food sources, intakes, stability and bioavailability and their protective role in humans. *Molecular Nutrition & Food Research* 53:194–218.
- Malewski W, Markakis P. 1971. Ascorbic acid content of the developing tomato fruit. *Journal of Food Science* 36:537–577.
- Marti R, Rosello S, Cebolla-Cornejo J. 2016. Tomato as a source of carotenoids and polyphenols targeted to cancer prevention. *Cancers (Basel)* 8:58. doi: [10.3390/cancers8060058](https://doi.org/10.3390/cancers8060058).
- Martin R, Villegas I, Sanchez Hidalgo M. 2006. Effects of resveratrol, a phytoalexin derived from red wines, on chronic inflammation induced in an experimentally induced colitis model. *British Journal of Pharmacology* 147:873–885.
- Martin-Pedraza L, Gonzalez M, Gomez F, Blanca-Lopez N, Garrido-Arandia M, Rodriguez R. 2016. Two nonspecific lipid transfer proteins (nsLTPs) from tomato seeds are associated to severe symptoms of tomato-allergic patients. *Molecular Nutrition & Food Research* 60:1172–1182. Pmid: 26840232.
- Matas AJ, Gapper NE, Chung MY, Giovannoni JJ, Rose JK. 2009. Biology and genetic engineering of fruit maturation for enhanced quality and shelf-life. *Current Opinion in Biotechnology* 20:197–203. doi: [10.1016/j.copbio.2009.02.015](https://doi.org/10.1016/j.copbio.2009.02.015).
- Mathieu S, Cin VD, Fei Z, Li H, Bliss P, Taylor MG. 2009. Flavour compounds in tomato fruits: identification of loci and potential pathways affecting volatile composition. *Journal of Experimental Botany* 60:325–337. doi: [10.1093/jxb/ern294](https://doi.org/10.1093/jxb/ern294).
- Modi B. 2019. Phytochemical analysis and nutritional value determination of *Tinospora cordifolia*. Masters Degree, Tribhuvan University, Kirtipur, Kathmandu, Nepal.

- Mohanty I, Joshi S, Trivedi D, Srivastava S, Gupta SK. 2002. Lycopene prevents sugar-induced morphological changes and modulates antioxidant status of human lens epithelial cells. *British Journal of Nutrition* 88:347–354. doi: [10.1079/BJN2002659](https://doi.org/10.1079/BJN2002659).
- Montonen J, Knekt P, Jarvinen R, Reunanen A. 2004. Dietary antioxidant intake and risk of type 2 diabetes. *Diabetes Care* 27:362–366. doi: [10.2337/di-acare.27.2.362](https://doi.org/10.2337/di-acare.27.2.362).
- Naidu K. 2003. Vitamin C in human health and disease is still a mystery. *Nutrition Journal* 2:14–19. doi: [10.1186/1475-2891-2-7](https://doi.org/10.1186/1475-2891-2-7).
- Nakagawa K, Kiko T, Hatade K, Sookwong P, Arai H, Miyazawa T. 2009. Antioxidant effect of lutein towards phospholipid hydro-peroxidation in human erythrocytes. *British Journal of Nutrition* 102:1280–1284. doi: [10.1017/S0007114509990316](https://doi.org/10.1017/S0007114509990316).
- Nguyen ML, Schwartz SJ. 1999. Lycopene: chemical and biological properties. *Food Technology* 53:38–45.
- Nishiumi S, Miyamoto S, Kawabata K. 2011. Dietary flavonoids as cancer-preventive and therapeutic biofactors.
- Nkondjock A, Ghadirian P, Johnson KC, Krewski D. 2005. The Canadian cancer registries epidemiology research group, dietary intake of lycopene is associated with reduced pancreatic cancer risk. *Journal of Nutrition* 135:592–597.
- Olson RE. 1999. Water soluble vitamins in principles of pharmacology.
- Paiva SAR, Russell RM. 1999. β -carotene and other carotenoids as antioxidants. *Journal of the American College of Nutrition* 18:426–433.
- Palan P, Naz R. 1996. Changes in various antioxidant levels in human seminal plasma related to immunofertility. *Archives of Andrology* 36:139–432.
- Pandey M, Shrestha J, Subedi S, Shah KK. 2020. Role of nutrients in wheat (*Triticum aestivum* L.): A review. *Tropical Agro Biodiversity* 1:18–23.
- Parajuli S, Pun NT, Parajuli S, Pandit JN. 2012. Antioxidant activity, total phenol and flavanoid contents in some selected medicinal plants of Nepal. *Journal of Health and Allied Sciences* 2:27–31.
- Paran E, Novack V, Engelhard YN, Hazan-Halevy I. 2009. The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients. *Cardiovascular Drugs and Therapy* 23:145–151.
- Pem D, Jeewon R. 2015. Fruit and vegetable intake: benefits and progress of nutrition education interventions- narrative review article. *Iranian Journal of Public Health* 44:1309–1321.
- Peralta IE, Spooner D. 2007. History, origin and early cultivation of tomato (Solanaceae). Genetic improvement of Solanaceous crops. In: Razdan MK, Mattoo AK, editors. *Genetic Improvement of Solanaceous crops*. Enfield Nueva Hampshire: Science Publishers 2:1–27.
- Porrini M, Riso P, Brusamolino A, Berti C, Guarnieri S, Visioli F. 2005. Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection. *British Journal of Nutrition* 93:93–99.
- Prasad NR, Karthikeyan A, Karthikeyan S, Reddy BV. 2011. Inhibitory effect of caffeic acid on cancer cell proliferation by oxidative mechanism in human ht-1080 fibrosarcoma cell line. *Molecular and Cellular Biochemistry* 349:11–19.
- Raiola A, Rigano MM, Calafiore R, Frusciante L, Barone A. 2014. Enhancing the health-promoting effects of tomato fruit for biofortified food. *Mediators Inflammation* doi: [10.1155/2014/139873](https://doi.org/10.1155/2014/139873).
- Ranjan A, Ichihashi Y, Sinha NR. 2012. The tomato genome: implications for plant breeding, genomics and evolution. *Genome Biology* 13:1–17.
- Rao AV, Agarwal S. 1998. Effect of diet and smoking on serum lycopene and lipid peroxidation. *Nutrition Research* 18:713–21.
- Rao AV, Rao LG. 2004. Lycopene and human health. *Current Topics in Nutraceutical Research* 2:127–36.
- Rao AV, Ray MR, Rao LG. 2006. Lycopene. *Advances in Food and Nutrition Research* 51:99–164.
- Rao V, Rao LG. 2007. Carotenoids and human health. *Pharmacological Research* 55:207–216.
- Richer S, Stiles W, Statkute L. 2004. Double-masked, placebo controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial). *Optometry* 75:216–230.
- Riso P, Visioli F, Grande S. 2006. Effect of a tomato-based drink on markers of inflammation, immunomodulation, and oxidative stress. *Journal of Agricultural and Food Chemistry* 54:2563–2566.

- Rissanen T, Voutilainen S, Nyyssonen K, Salonen JT. 2002. Lycopene, atherosclerosis and coronary heart disease. *Experimental Biology and Medicine* 227:900–907.
- Rodriguez JA, Nespereira B, Perez-Illzarbe M, Eguinoa E, Paramo JA. 2005. Vitamins C and E prevent endothelial VEGF and VEGFR-2 overexpression induced by porcine hypercholesterolemic LDL. *Cardiovascular Research* 65:665–673.
- Sablani SS, Opara LU, Al-Balushi K. 2006. Influence of bruising and storage temperature on vitamin C content of tomato fruit. *Journal of Food Agriculture and Environment* 4:54.
- Safari MR. 2007. Effects of lycopene on the susceptibility of low density lipoproteins to oxidative modification. *Iranian Journal of Pharmaceutical Research* 6:173–177.
- SanGiovanni JP, Chew EY, Clemons TE. 2007. The relationship of dietary carotenoid and vitamin A, E, and C intake with age-related macular degeneration in a case-control study. *AREDS report* 125:1225–1232.
- Seabra RM, Andrade PB, Valentao P, Fernandes E, Carvalho F, Bastos ML. 2006. *Molecules in Biomaterials From Aquatic and Terrestrial Organisms*. Science Publishers, Enfield, NH, USA.
- Serio F, Leo L, Parente A, Santamaria P. 2007. Potassium nutrition increases the lycopene content of tomato fruit. *Journal of Horticultural Science and Biotechnology* 82:941–945. doi: [10.1080/14620316.2007.11512330](https://doi.org/10.1080/14620316.2007.11512330).
- Seymour GB, Chapman NH, Chew BL, Rose JKC. 2013. Regulation of ripening and opportunities for control in tomato and other fruits. *Plant Biotechnology* 11:269–278. doi: [10.1111/j.1467-7652.2012.00738.x](https://doi.org/10.1111/j.1467-7652.2012.00738.x).
- Shahidi F, Janitha PK, Wanasundara PD. 1992. Phenolic antioxidants. *Critical Reviews in Food Science and Nutrition* 32:67–103.
- Sharoni Y, Danilenko M, Dubi N, Ben-Dor A, Levy J. 2004. Carotenoids and transcription. *Archives of Biochemistry and Biophysics* 430:89–96.
- Shi J, LeMaguer M, Niekamp F. 1999. Lycopene degradation and isomerization in tomato dehydration. *Food Research* 32:15–21.
- Shinozaki Y, Nicolas P, Fernandez-Pozo N, Ma Q, Evanich D, Shi Y. 2018. High-resolution spatiotemporal transcriptome mapping of tomato fruit development and ripening. *Nature Communications* 9:364. doi: [10.1038/s41467-017-02782-9](https://doi.org/10.1038/s41467-017-02782-9).
- Shrestha J, Kandel M, Subedi S, Shah KK. 2020a. Role of nutrients in rice (*Oryza sativa* L.): a review. *Indian Journals* 9:53–62. doi: [10.5958/2394-448X.2020.00008.5](https://doi.org/10.5958/2394-448X.2020.00008.5).
- Shrestha J, Shah KK, Timsina K. 2020b. Effects of different plant fertilizers on growth and productivity of rice (*Oryza sativa* L.): a review. *International Journal of Global Science Research* 7:1291–1301. doi: [10.26540/ijgsr.v7.i1.2020.151](https://doi.org/10.26540/ijgsr.v7.i1.2020.151).
- Silaste ML, Alfhan G, Aro A, Kesaniemi YA, Horkk. 2007. Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation. *British Journal of Nutrition* 98:1251–1258.
- Solini E, Santini F, E. 2006. Effect of short-term folic acid supplementation on insulin sensitivity and inflammatory markers in overweight subjects. *International Journal of Obesity* 30:1197–1202.
- Sporn MB, Liby KT. 2013. Is lycopene an effective agent for preventing prostate cancer. *Cancer Prevention Research* 6:384–386.
- Stahl W. 2006. *Tomato lycopene in photo protection and skin care*. volume 60. Caledonian Science Press, Scotland.
- Stahl W, Heinrich U, Wiseman S, Eichler O, Sies H, Tronnier H. 2001. Dietary tomato paste protects against ultraviolet light induced erythema in humans. *Journal of Nutrition* 131:1449–1451.
- Stahl W, Sies H. 2003. Antioxidant activity of carotenoids. *Molecular Aspects of Medicine* 24:345–351.
- Suresh BV, Roy R, Sahu K, Misra G, Chattopadhyay D. 2014. Tomato genomic resources database: an integrated repository of useful tomato genomic information for basic and applied research. *PLoS One* 9:86387. doi: [10.1371/journal.pone.0086387](https://doi.org/10.1371/journal.pone.0086387).
- Takeoka GR, Dao L, Flessa S, Gillespie DM, Jewell WT, Huebner B, Bertow D, Ebeler S. 2001. Processing effects on lycopene content and antioxidant activity of tomatoes. *Journal of Agricultural and Food Chemistry* 49:3713–3717.
- Tamasi G, Pardini A, Bonechi C, Donati A, Pessina F, Marcolongo. 2019. Characterization of nutraceutical components in tomato pulp, skin and locular gel. *European Food Research and Technology* 245:907–918. doi: [10.1007/s00217-019-03235-x](https://doi.org/10.1007/s00217-019-03235-x).
- Tiwari I, Shah KK, Tripathi S, Modi B, Shrestha J, Pandey HP, Bhattarai BP, Rajbhandari BP. 2020. Post-harvest practices and loss assessment in tomato (*Solanum lycopersicum* L.) in Kathmandu, Nepal. *Journal of Agriculture and Natural Resources* 3:335–352. doi: [10.3126/janr.v3i2.32545](https://doi.org/10.3126/janr.v3i2.32545).

- Tohge T, Fernie AR. 2015a. Metabolomics-inspired insight into developmental, environmental and genetic aspects of tomato fruit chemical composition and quality. *Plant and Cell Physiology* 56:1681–1696. doi: [10.1093/pcp/pcv093](https://doi.org/10.1093/pcp/pcv093).
- Tohge T, Fernie AR. 2015b. Metabolomics-inspired insight into developmental, environmental and genetic aspects of tomato fruit chemical composition and quality. *Plant and Cell Physiology* 56:1681–1696. doi: [10.1093/pcp/pcv093](https://doi.org/10.1093/pcp/pcv093).
- Tohge T, LP, Fernie A. 2017. Current understanding of the pathways of flavonoid biosynthesis in model and crop plants. *Journal of Experimental Botany* 68:4013–4028. doi: [10.1093/jxb/erx177](https://doi.org/10.1093/jxb/erx177).
- van Bennekum A, Werder M, Thuahnai ST, Han CH, Duong P, Williams DL, Wettstein P, Schulthess G, Phillips MC, Hauser H. 2005. Class B Scavenger Receptor-Mediated Intestinal Absorption of Dietary β -Carotene and Cholesterol. *Biochemistry* 44:4517–4525. doi: [10.1021/bi0484320](https://doi.org/10.1021/bi0484320).
- Viuda-Martos M, Sanchez-Zapata E, Sayas-Barbera E, Sendra E, Perez-Alvarez JA, Fernandez-Lopez J. 2014. Tomato and tomato byproducts. human health benefits of lycopene and its application to meat products: a review. *Critical Reviews in Food Science and Nutrition* 54:1032–1049. doi: [10.1080/10408398.2011.623799](https://doi.org/10.1080/10408398.2011.623799).
- Wagner C. 1995. Biochemical role of folate in cellular metabolism in Folate in Health and Disease. 4 edn edition. New York, NY, USA: Marcel Dekker.
- Wals P, Tairou F, VanAllen MI. 2007. Reduction in neural tube defects after folic acid fortification in Canada. *The New England Journal of Medicine* 357:135–142.
- Wang Y, Luo Z, Lu C, Zhou R, Zhang H, Zhao L. 2019. Transcriptome profiles reveal new regulatory factors of anthocyanin accumulation in a novel purple-colored cherry tomato cultivar Jinling Moyu. *Plant Growth Regulation* 87:9–18. doi: [10.1007/s10725-018-0444-y](https://doi.org/10.1007/s10725-018-0444-y).
- Wilcox JK, Catignani GL, Lazarus C. 2003. Tomatoes and cardiovascular health. *Critical Reviews in Food Science and Nutrition* 43:1–18.
- Wood M. 2001. New clues about carotenes revealed. *Agricultural Research* 49:12–12.
- Yahia EM, Contreras-Padilla M, Gonzalez-Aguilar G. 2001. Ascorbic acid content in relation to ascorbic acid oxidase activity and polyamine content in tomato and bell pepper fruits during development, maturation and senescence. *LWT—Food Science and Technology* 34:452–457.
- Zanor MI, Rambla JL, Chaib J, Steppa A, Medina A, Granell A. 2009. Metabolic characterization of loci affecting sensory attributes in tomato allows an assessment of the influence of the levels of primary metabolites and volatile organic contents. *Journal of Experimental Botany* 60:2139–2154. doi: [10.1093/jxb/erp086](https://doi.org/10.1093/jxb/erp086).
- Zechmeister L, LeRosen AL, Went FW, Pauling L. 1941. Prolycopene, a naturally occurring stereoisomer of lycopene. *Proceedings of the National Academy of Sciences of the United States of America* 21:468–74.
- Zhou R, Kong L, Wu Z, Rosenqvist E, Wang Y, Zhao L. 2019. Physiological response of tomatoes at drought, heat and their combination followed by recovery. *Physiologia Plantarum* 165:144–154.



© 2021 by the author(s). This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0) License



The Official Journal of the **Farm to Fork Foundation**
ISSN: 2518–2021 (print)
ISSN: 2415–4474 (electronic)
<http://www.f2ffoundation.org/faa>