International Journal of Cell Science and Biotechnology
E-ISSN 2320-7574
https://ijcsb.evegenis.org/

Original Review Article

Bioactive Compounds in Tomatoes and Their Effects on Human Health -A Comprehensive Review

Haroon Rasheed[1], Aurida Javed[1], Ayesha Haroon[2] and Somavia Ameen*

[1]Institute of Food Science and Technology, University of Agriculture Faisalabad, Pakistan
*[2]Department of Chemistry, Government College University Faisalabad, Pakistan

Received 26 September2022, Accepted 05 December 2022, Available online 10 December2022, **Vol.12, No.2 (November/December2022)**

Abstract

Bioactive compounds are the constituents of foods, especially functional foods that provide beneficial health properties. For example, these benefits include antioxidants, anti-inflammatory, antifungal, and various additional preventative properties, which illustrates how bioactive compounds are the real-life example of Hippocrates' notion "let thy food be thy medicine". Originally, many definitions of functional foods neglected to acknowledge the importance of bioactive compounds. Many of these compounds have antioxidant activities and are effective in protecting the human body against various oxidative stress-related diseases. Dietary tomatoes increase the body's level of antioxidants, trapping reactive oxygen species and reducing oxidative damage to important biomolecules such as membrane lipids, enzymatic proteins and DNA, thereby ameliorating oxidative stress. We reviewed the nutritional and phytochemical compositions of tomatoes. In addition, the impacts of the constituents on human health, particularly in ameliorating some degenerative diseases, are also discussed. Moreover, tomato and its bioactive components hold potential to become effective modules in diet-based regimens; however, integrated research and meta-analysis are still required to enhance meticulousness.

Keywords: *Tomato, Bioactive compounds, antioxidants, Health benefits, metabolism and absorption.*

Introduction

Fruits and vegetables are gaining immense importance in the domain of nutrition owing to presence of vital phytochemicals and bioactive molecules. Their health promoting potentials are due to presence of functional ingredients, e.g., polyphenols, flavonoids, tannins, anthocyanins, etc [1]. These compounds trigger and alter body metabolism and modulate detoxification mechanism. Thereby, provide protection against lifestyle disorders, cancer insurgence, etc. Nevertheless, antiox. idant potential of fruits and vegetables varies thus their balanced consumption is better than reliance on few specific groups [2].

Tomatoes (Solanum lycopersicum L.), which are frequently included in the Mediterranean diet and are widely consumed as vegetables, play an important role in nutrition because of their well-established health benefits [3]. Tomatoes are used in many processed food products such as sauces, salads, soups, and pastes [4].

Common nutrients reported to be present in tomatoes are vitamins, minerals, fiber, protein, essential amino acids, monounsaturated fatty acids, carotenoids and phytosterols [5–7]. These nutrients perform various body functions including constipation prevention, reduction in high blood pressure, stimulation of blood circulation, maintenance of lipid profile and body fluids, detoxification ofbody toxins and maintaining bone structure as well as strength [1,7,8]. Tomatoes are also an excellent source of nutrients and bioactive compounds, commonly known as secondary metabolites, the concentrations of which are correlated with the prevention of human chronic degenerative diseases, such as cardiovascular disease (CVD), cancer, and neurodegenerative diseases [9–11].

Due to the high concentrations of different natural antioxidant chemicals, such as carotenoids (β-carotenoids and lycopene), ascorbic acid (vitamin C), tocopherol (vitamin E) and bioactive phenolic compounds (quercetin, kaempferol, naringenin and lutein, as well as caffeic, ferulic and chlorogenic acids), tomatoes can help ameliorate many diseases, especially chronic diseases [12-13]. These compounds play beneficial roles in inhibiting reactive oxygen species (ROS) by scavenging free radicals, inhibiting cellular proliferation and damage, inhibiting apoptosis as well as metal chelation, modulation of enzymatic activities, cytokine expression and signal transduction

*Corresponding author's ORCID ID: 0000-0003-1121-7224
DOI: https://doi.org/10.14741/ijcsb/v.11.1.3

pathways [12,14]. The main carotenoid in tomato is lycopene, which is responsible for its red color. The pharmacological activities of lycopene and other phenolic compounds include anticancer, anti inflammatory, antidiabetic, anti-allergenic, anti atherogenic, antithrombotic, antimicrobial, antioxidant, vasodilator and cardioprotective effects [15–18].

In addition to having good nutritive value and health promoting activities, the polyphenolic compounds and carotenoids also contribute to sensory activities including maintaining good aroma, taste, and texture [19]. Tomato is an important dietary source of both soluble and insoluble dietary fibers, namely cellulose, hemicelluloses and pectins [20]. In general, hese fibers are resistant to intestinal digestion in the large intestine and are believed to ameliorate bowel disorders, cancer, diabetes, CVDs, and obesity [21,22].

The definition of functional foods is not regulated. Accordingly, many institutions have individual definitions. There is no one definition of functional foods accepted by all. Functional foods are generally defined as those that improve health and can help treat disease. The Functional Food Center previously defined functional foods as "Natural or processed foods that contain known or unknown biologically active compounds; which, in defined, effective, and non-toxic amounts, provide a clinically proven and documented health benefit for the prevention, management, or treatment of chronic diseases" [23]. However, in 2017, the Functional Food Center updated their definition to: "natural or processed foods that contain biologically active compounds which, in defined, effect, and non-toxic amounts provide clinically proven and documented health benefit utilizing specific biomarker for the prevent, management, or treatment of chronic disease or its symptoms" [23-25].

The new change removes the notion of the unknown compounds, which acknowledges that there are bioactive compounds. Additionally, there is acknowledgement that bioactive compounds can also be instrumental in treating symptoms, not just the management of chronic disease. Countless studies on functional foods show "the intake of selected foods and their associated constituents can have profound physiologic effects." These effects are driven by the bioactive compounds in the functional foods [26]. Bioactive compounds have specific health benefits that contribute to the function of functional foods and should therefore be included the definition of functional foods. Many institutions have their own definition of functional foods, as there is no regulated standard definition. For example, the Institute of Food Technologists define these foods as "foods and food components that provide a health benefit beyond basic nutrition. These substances provide essential nutrients often beyond quantities necessary for normal maintenance, growth, and development, and/or other biologically active components that impact health benefits" [25].

While this definition does mention biologically active components, there is a failure to discuss the important aspects of bioactive compounds that further ensure health. More specifically, there is no discussion of toxicity of an excess of bioactive compounds or a minimum level in the diet to obtain the benefits. Without the proper inclusion of bioactive compounds, the definition does not identify the important aspect of functional foods that interact with the biomarkers and improve health. The advancement in the Functional Food Center's definition generates a clearer notion of the mechanism of functional foods by identifying that bioactive compounds work on biomarkers, which indicate effectiveness [27-29].

A functional food, previously defined, is a food containing biologically active compounds that can be used to treat a disease and/or its symptoms. With the rise of chronic disease, effective treatment is in high demand [2]. The concept was originally introduced by the Japanese, with the idea that certain foods can work beyond mundane nutritional effects [26]. Functional foods target specific mechanisms that are linked to chronic diseases such as cancer and Alzheimer's disease [30]. Through targeting these mechanisms, functional foods accomplish what medication often fails to do: treat chronic disease. Functional foods, if they are consumed under the toxic dosage, effectively manage chronic diseases and their accompanied symptoms, without the excessive side effects that are associated with medication. However, medication frequently brings adverse side effects while functional foods, using bioactive compounds, can treat disease. [31-32].

Type 2 Diabetes is not the only chronic disease that has been treated with functional foods. Several studies have explored the use of functional foods for the treatment of cardiovascular diseases. For For example, seaweed, a functional food candidate, is used as a preventative measure in the treatment those at risk of heart disease [33]. Algae metabolites, such as lipids and fiber, act as bioactive compounds that interact with biological aspects. These interactions in turn provide protective properties against cardiovascular diseases [34]. It has even been investigated Use of functional foods in the treatment, prevention and management of cancer. many herbs Remedies such as the leaves and bark are considered functional foods. Cancer patients have been using these herbal remedies to control cancers, including breast, colon, and prostate. The Functional food remedies have been clinically shown to help these patients in the management, solidifying the importance of functional foods in the management of chronic diseases [9]. the bioactive compounds are the main source of functional foods capable of treating, managing and preventing chronic disease. Consequently, bioactive compounds must be recognized to fully understand the concept of functional foods [34-35].

Bioactive compounds interact with biomarkers. By doing this, these compounds can improve the quality of life of people, which is exhibited in clinical research. Bioactive compounds are the driving force that establishes the functional aspect of functional foods. a standard Recognition of these compounds will bring a general understanding of how functional Food improves health. Therefore, the updated definition of the Center for Functional Foods is a step in the right direction. direction. Bioactive compounds play a fundamental role in functional foods as a component that improves health and helps treat diseases [36-38].

Tomato Plant Overview

Tomato (Solanum lycopersicum) typically red fruit belongs to the nightshade family having 1–3 meters (3–10 ft) in height with weak stem that often sprawls over the ground and may vines over other plants. It is perennial plant often grow outdoors in temperate climates. The tomato fruit is consumed in diverse ways, including raw, as an ingredient in many dishes and sauces, and in drinks. It is botanically a fruit and only considered as vegetable during culinary purposes that cause some confusion. The fruit is rich in lycopene, which may have beneficial health effects. Tomatoes and tomato-based food products are the major source of lycopene and a number of other carotenoids, such as phytoene, phytofluene, α-carotene, β-carotene, gammacarotene, and neurosporene. While tomato-based products are reported to be the primary source of dietary lycopene in the United States. Over the past decade, there has been increasedinterest in the health benefits of lycopene consumption [39-40].

Structure and formation of carotene

Lycopene is defined chemically as an acyclic carotene with 11 conjugated double bonds, normally present in the alltransconfiguration. The double bonds are subject to isomerization, and various cis isomers are found in plants and also in blood plasma. Since the human body is unable to synthesize carotenoids endogenously so the body is totally dependent on dietary source carotenoids. In general, 85% of dietary lycopene in human diet is coming from tomato fruit and tomato-based food products [41].

Carotenoids like lycopene are important pigments found in plants, photosynthetic bacteria, fungi, and algae. They are responsible for the bright colors of fruits and vegetables and protection of photosynthetic organisms from excessive light damage. Lycopene is a key intermediate in the biosynthesis of many important carotenoids, such as β carotene, and xanthophylls. Formation of β caroteine begins with mevalonic acid conversion into dimethylallyl pyrophosphate followed by condensation with three molecules of isopentenyl pyrophosphate and to give geranylgeranyl pyrophosphate. Moreover, two molecules of this product further condensed tail-to-tail to give 40 carbon phytoene. Through several desaturation steps, phytoene is converted into lycopene and then two terminal isoprene groups can be cyclized to produce β carotene that can then be transformed into a wide variety of xanthophylls [44]. An illustration of the formation of β-carotene has been given in the Fig. 1.

Tomato also contains trace amount of saturated, polyunsat- urated fatty acids, and free cholesterols which help to prevent many heart diseases. Lavelli et al. (2000) reported that tomato pulp contains some essential amino acids while its seeds have higher amounts of minerals (Fe, Mn, Zn, and Cu). They also have monounsaturated fatty acids especially oleic acid and linolenic acid. Aspratic acid, gultamic acid have highest amount present in tomato 0.16 and 0.42 mg, respectively, mentioned in Table 2.

Table1 Nutritionalprofileoftomatoes

Nutrient	Valueper100g
Water	94.78
Protein	1.167
Totallipids	0.19
carbohydrate	3.18
Mineralsmg/100g	
Calcium(Ca)	5
Magnesium(Mg)	8
Phosphorus(P)	29
Potassium(K)	212
Sodium(Na)	42
Zinc(Zn)	0.14
Manganese(Mn)	0.088
Totaldietary	0.9
Vitaminsmg/100g	
VitaminC,totalascorbicacid	16
Thiamin	0.046
Riboflavin	0.034
Niacin	0.059
Pantothenicacid	0.018
VitaminB-6	0.06

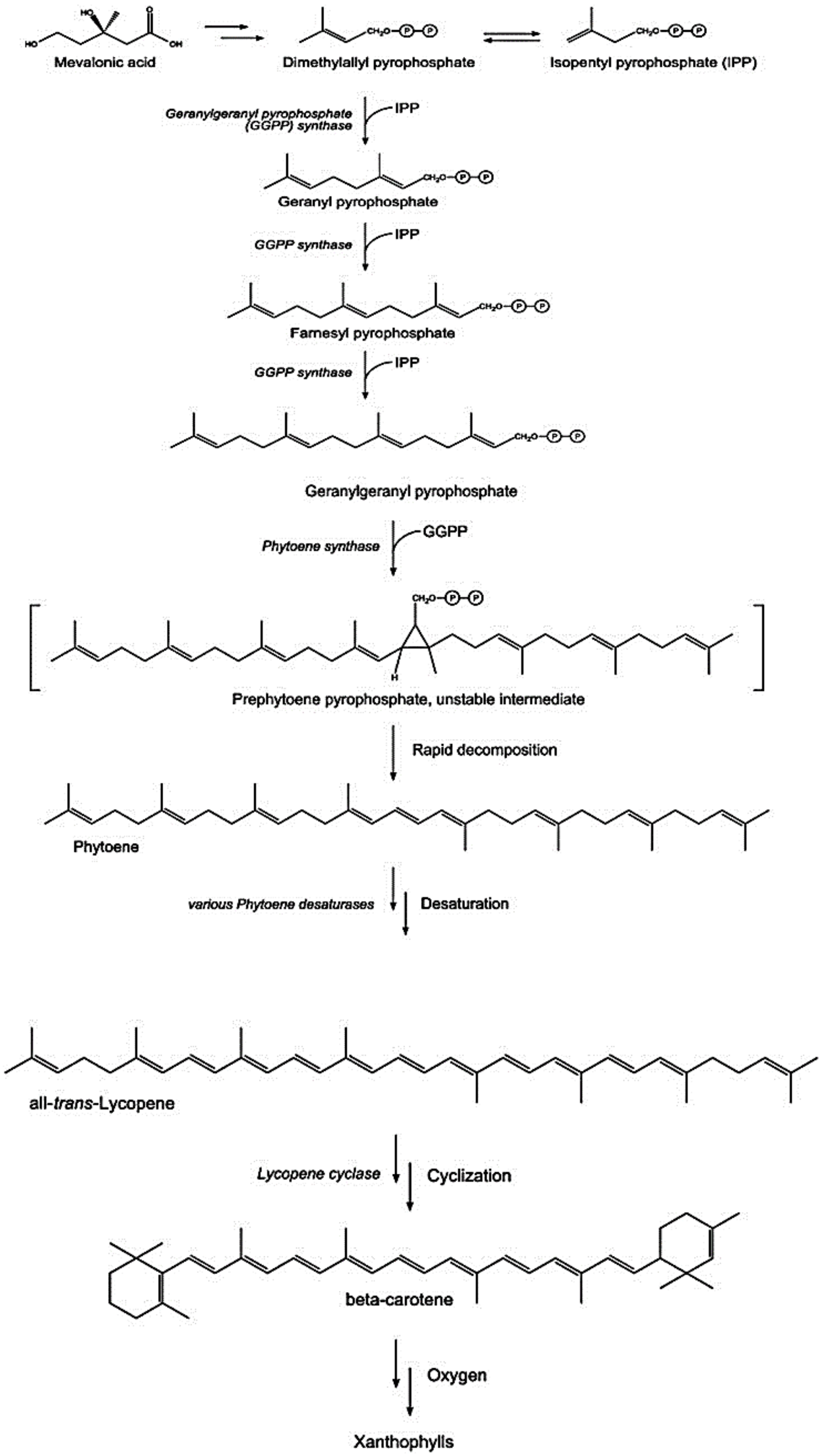

Figure 1 Formation of β-carotene

Table 2 Amino acids and fatty acids profile of tomatoes fruit

Tryptophan	0.008
Threonine	0.029
Isoleucine	0.027
Leucine	0.042
Lysine	0.042
Methionine	0.010
Cystine	0.015
Phenylalanine	0.030
Tyrosine	0.020
Valine	0.030
Arginine	0.029
Histidine	0.018

Methodology

A comprehensive literature search was performed by combining the appropriate key- words including "tomato", "nutritional composition", "proximate composition", "phyto- chemicals", "physiochemical properties", "mineral", "vitamin", "fatty acid", "amino acid", "carotenoid", "phytosterol", "antioxidant properties", "bioactive compounds", "health ben- efits", "human degenerative diseases", "cardiovascular diseases", "diabetes" and "can- cer". As for the search engine, Google Scholar, Scopus, Web of Science, ScienceDirect, and Pubmed were independently searched. Only English language published articles were considered. There was no year restriction, and the final search was conducted on 27 July 2020. The references were managed with EndNote software (version X7).

Proximate Composition

Proximate analysis is one of the first approaches for food characterization, particularly for the identification of nutrients in any food products. Generally, water, ash, protein, lipid, carbohydrate, sugar and reducing sugar contents, as well as pH, energy and acidity are the key proximate compositions of a food sample [42]. For instance, ash content is an important step in the analysis of nutritional element contents in food products. Ash refers to the inorganic residue (mineral content) that remains after the complete oxidation of organic matter and removal of water by heating (ashing) of a food sample in a furnace [43-46]. Next, moisture content (total solids) is important because it affects the chemical and physical aspects of food, which determine its freshness and storage stability [47,48]. Protein, lipids, and carbohydrates are principal components of foods and are the main elements in proximate composition analysis.

Proteins, which are macromolecules present in food, are important for cellular struc- ture and biological functions. Protein analysis is crucial for nutritional labeling, as well as in describing the biological activities and functional properties of food products [49]. Lipids are another group of macromolecules that are generally insoluble in water but are soluble in organic solvents. In fact, precise and accurate analysis of lipid content in food is mandatory for the standard of quality and nutritional labeling and is important in ensuring manufacturing specification [50].

Carbohydrate analysis is also important as a major (more than 70%) energy source. Carbohydrate analysis yields nutritional information, standard of identity, water holding capacity, flavors, desirable textures, and stability of food products [48]. In addition, pH analysis of food samples is essential for food processing and storage. Dietary fiber is another important component of proximate analysis because it ensures a variety of health benefits, including protection against heart disease, colon cancer and diabetes [51]. In a more recent study based on previously published original research articles, an average tomato consists of ash 8.75%, water 94.17 (g/100 g), moisture 91.18 (g/100 g), total pro- tein 17.71 (g/100 g), lipid 4.96 (g/100 g), carbohydrates 5.96 (g/100 g), total sugar 50.60 (g/100 g), pH 3.83, energy 34.67 kcal/100 g, acidity 0.48%, reducing sugar 35.84%, fruc- tose 2.88%, glucose 2.45%, sucrose 0.02% and total fiber 11.44 (g/100 g).

Mineral Content

Minerals are naturally occurring inorganic solid substances. They are essential for a variety of bodily functions, including the regulation of metabolic pathways, formation of vital organs, maintenance of bodily physiological functions, regulation of pH balance, fluid balance, blood pressure, nerve transmission, muscle contraction and energy production [53–56]. Some minerals, such as calcium (Ca), potassium (K), sodium (Na), phosphorus (P), magnesium (Mg), sulfur (S) and chlorine (Cl), are highly essential (average daily intake >50 mg) and are therefore known as major elements. Others include iron (Fe), iodine (I), zinc (Zn), fluorine (F), copper (Cu), selenium (Se), manganese (Mn), cobalt (Co), chromium (Cr), nickel (Ni), molybdenum (Mo) and selenium (Se), which are required in comparatively smaller amounts (< 50 mg/day) and are known as trace elements. Other elements, such as aluminum (Al), arsenic (As), boron (B), barium (Ba), bismuth (Bi), bromine (Br), lead (Pb), cadmium (Cd), cesium (Cs), germanium (Ge), lithium (Li), mercury (Hg), rubidium (Rb), silicon (Si), antimony (Sb), tin (Sn), samarium (Sm), strontium (Sr), tungsten (W), tita- nium (Ti) and thallium (Tl), which are needed in even smaller amounts, (1 μg/day) are known as ultratrace elements [57–59]. Pb, As, Hg, Cd, Cu, Cr, Ni, Zn and Mn are heavy metals that are toxic if present in low concentrations because they tend to accumulate in living cells [59,60]. From a nutritional perspective, tomato is a good source of minerals and other ele- ments [4,44]. In this review, 23 types of minerals and their amounts present in tomato are compiled, including the major elements (calcium, potassium, sodium, phosphorus, magne- sium, sulfur, chlorine) and trace elements (iron, iodine, zinc, fluorine, cupper, manganese, cobalt, chromium, nickel, aluminum, arsenic, boron, lead, cadmium, nitrate, chlorine, selenium, silicon) (Table 3).

Table 3

Elements	Units	Concentrations	Range
Sodium (Na)	mg/100 g	70.38 ± 12.20	56.90–80.65
Boron (B)	µg/g	36.83 ± 3.27	25.84–48.59
Nickel (Ni)	mg/100 g	0.66 ± 0.00	0.66
Nitrate(NO_3)	mg/100g	274.37±156.75	86.21–459.00
Iron (Fe)	mg/100g	4.55±2.18	1.50–6.45
Zinc(Zn)	mg/100g	2.48±1.05	0.17–3.17
Cobalt(Co)	mg/100g	19.66±9.66	10.00-29.31
Copper(Cu)	mg/100g	0.67±0.15	0.06–1.10
Manganese(Mn)	mg/100g	0.60±0.12	0.11–1.88
Chromium(Cr)	µg/100g	193.80±133.80	60.00–327.59
Iodine(I)	mg/100g	2.65±1.44	0.18–3.97
Fluorine(F)	µg/100g	413.79±0.00	413.79
Aluminum(Al)	µg/100g	1241.38±0.00	1241.38
Silicon(Si)	µg/100g	46.55±0.00	46.55
Selenium(Se)	µg/100g	13.45±3.45	10.00–16.90
Lead(Pb)	µg/g	1.21±0.06	1.15–1.27
Cadmium(Cd)	µg/g	0.17±0.06	0.11–0.22
Arsenic(As)	µg/g	0.20±0.005	0.19–0.20

Concentrations are expressed as mean±standard deviation

Vitamin content

The accurate and precise analysis of vitamin content is important for a standard balanced diet because low or excessive amounts of vitamins can contribute to disease conditions by hampering normal cell growth [64]. Tomatoes are one of the most versatile and widely consumed vegetables in many countries and are a rich source of vitamins [65,66]. Vitamins C, B-complex, A, E and K are the main types of vitamins present in tomato, with vitamin C reported to be the highest (Table 4).

Table 4

Vitamins	Units	Concentrations	Range	References
Vitamin A	IU/100 g	614.44 ± 248.18	267.33–833.00	[4,46,61,62, 65,69,73–76]
Vitamin E	µg/100 g	15.08 ± 1.06	14.02–16.13	
Vitamin K	µg/100 g	98.28 ± 0.00	98.28	
Vitamin C	mg/100 g	36.16 ± 29.64	10.86–85.00	
Thiamine	mg/100 g	0.66 ± 0.44	0.04–0.98	
Riboflavin	mg/100 g	0.48 ± 0.34	0.02–0.81	
Niacin	mg/100 g	9.68 ± 0.00	9.68	
Pantothenic Acid	mg/100 g	4.93 ± 0.41	4.52–5.34	
Vitamin B_6	mg/100 g	1.51 ± 0.22	1.29–1.72	
Biotin	µg/100 g	68.97 ± 0.00	68.97	
Folate	mg/100 g	14.00 ± 1.00	13.00–15.00	

Concentrations are expressed as mean ± standard deviation.

Vitamins C and E (tocopherol) exhibit antioxidant activities making tomato a useful therapeutic agent for the prevention of various diseases, including CVDs and cancer [12,67–70]. Among the various types of vitamin B-complexes, the amount of folate is comparatively high in tomatoes. Nevertheless, excessive amounts of water-soluble vitamin B do not cause any toxicity because these vitamins can be easily excreted from the body. Vitamins perform various functions, such as maintaining the nervous system, producing red blood cells and enzymatic function [71,72].

Health benefits of tomato

The health benefits of tomatoes mainly associated with its rich supply of nutrients and secondary metabolites, including vitamins, minerals, essential fatty acids, carotenoids, antioxidants, and other bioactive compounds. In addition to its high amounts of vitamins A, C, E, K and B-complex [5,37], tomato is also a good source of important minerals as previously stated [3,47]. Additionally, tomato contains some dietary fiber, protein, essen- tial amino acids, and a number of bioactive anti-oxidative organic compounds including lycopene, quercetin, kaempferol, naringenin, caffeic acid, rutin, resveratrol, catechin and luteolin, which contribute to the maintenance of good health [44]. Vitamins C and E are natural antioxidants that can prevent degenerative diseases caused by free radicals [74].

Lycopene is a natural antioxidant that can help combat different types of cancer, including prostate, breast, lung, stomach, colorectal, oral, esophageal, pancreatic, bladder, cervical and ovarian cancers [10,17]. Abundant amounts of minerals are responsible for maintenance of body's physiological functions including blood pressure, blood clotting, nerve transmission, muscle contraction and energy production [56,75], while the vitamins help to maintain the health of the nervous system, facilitate blood cell production and enzymatic function [77].

The consumption of carotenoid-rich tomato has been reported to protect against vitamin A deficiency disorders and other chronic diseases including light-induced eye damage, the development of cataracts and age-related macular degeneration [78]. In fact, a high dietary intake of carotenoids (lutein and zeaxanthin) can prevent the risk of age- related macular degeneration, making tomato useful in ameliorating eye diseases [74]. Other important constituents present in tomato are phytosterols, which prevent intestinal cholesterol absorption by displacing it from the micelles, and thus stimulating its excretion, preventing CVDs, and ameliorating different types of cancer including colon, prostate, and breast cancers [79].

Oxidative stress is the main contributor to the development of chronic diseases in humans. ROS, including superoxide anion radicals, hydroxyl radicals and hydrogen per- oxide, are highly reactive oxidant molecules that are endogenously induced by regular metabolic activity in the body, diet, and secondary lifestyle activities. They react with cellular components (DNA, lipids, and proteins) to cause oxidative damage [79]. Antioxidants are super-protective agents that inactivate ROS and prevent oxidative dam- age [130]. Natural antioxidants such as vitamins C and E, different types of carotenoids and phenolic compounds including quercetin, kaempferol, caffeic acid, naringenin, chloro- genic acid, lutin, ferulic acid, lycopene, resveratrol, catechin and luteolin are present in tomato [6,72]. These bioactive compounds will protect endogenously produced reactive oxidant molecules and prevent oxidative damage. Therefore, they prevent the development of different types of cancer, diabetes and cardiovascular, eye, hypertension, inflammatory and neurodegenerative diseases [80].

In summary, the health benefits of tomato are associated with its rich supply of nutrients to the body, such as minerals, vitamins, proteins, essential amino acids, fatty acids, and other antioxidants. The consumption of tomato is associated with the relief of cancer, diabetes, CVDs, eye disease and constipation, with blood pressure reduction, improved blood circulation, improved body fluid balance, cholesterol reduction, detoxification of toxins, reduction in inflammation, prevention of premature aging and improvement of digestive function (Figure 2).

Generally, CVD is a category of disease that affects the blood vessels and the heart [81]. Common predisposing factors include hypertension, gender, age, hypercholesterolemia, obesity, diabetes, and unhealthy lifestyle, such as minimal physical activity, smoking, the consumption of a high fat diet and excessive alcohol. The bioactive compounds in tomato not only reduce the risk but also prevent or ameliorate CVDs [82] (Figure 2). The antiplatelet aggregation effects of tomato and tomato products support the preven- tion of CVD disorders. For example, lycopene can improve endothelial function among patients who suffer from CVD [81]. Lycopene functions as a crucial hypolipi- demic and antioxidant agent and inhibits factors that play important prothrombosis and pro-inflammatory roles, and thus improves CVDs [71]. Additionally, it is hypothesized that lycopene can increase LDL degradation and reduce cholesterol synthesis. It has been reported that both the thickness of the intima wall and myocardial infarction (MI) can be minimized by high lycopene intake [82]. As a radical scavenger, lycopene mops up singlet oxygen along with other active free radicals, and thus protects against vascular cell damage, which contributes to CVD [77]. Lycopene also shows antiplatelet and antithrom- botic activities by hindering phospholipase C activation, which inhibits the breakdown of phosphoinositol and the formation of thromboxane B2. Subsequently, the mobilization of intracellular calcium, which is beneficial in CVDs, is impeded. In addition, the cyclic guano- sine monophosphate (cGMP) /nitrate formation in the platelets activated by lycopene also constrains platelet aggregation [83].

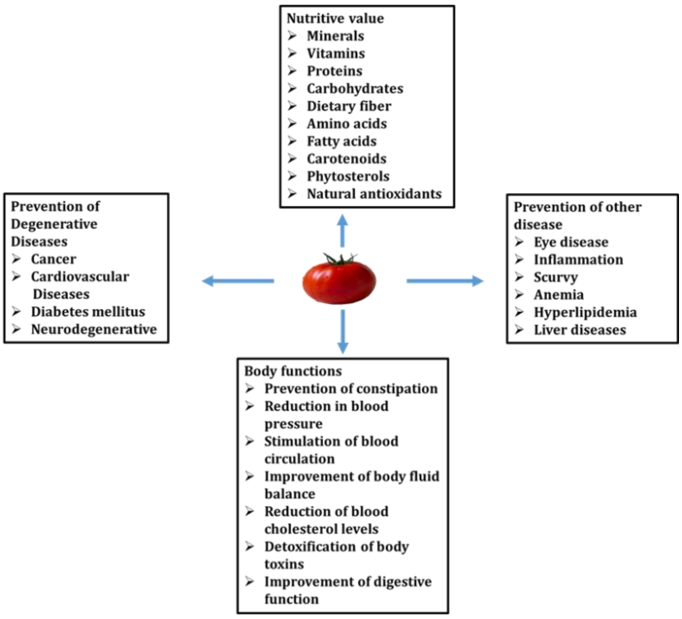

Figure 2 Summary of health benefits of tomato

Oxidative stress

The process of oxidation is essential in vitality of life coupled with production of ROS. A natural balance between ROS pro- duction and antioxidant defense system exist and its imbalance results in oxidative stress resulting in damage to membranes and cell constituents such as DNA, lipids, and proteins. The in- take of antioxidant rich diets or supplementation with bioactive molecules, like vitamins, carotenoids, and tannins may provide protection against oxidative damage [84].

Some researcher demonstrated that lycopene has antioxidative perspectives, which can prevent DNA dam- age and hence protect against mutations that cause cells cancer development. Furthermore, recent studies reflect that lycopene may also modify molecular biomarkers of atherosclerosis [84] while studies on the dose-dependent effects of lycopene have reported conflicting results. For instance, higher lycopene intake (20 mg lycopene/kg diet) from tomato paste was reported to improve plasma lipid profiles in rodent experimental modeling (Ibrahim et al., 2008). There have been several studies showing tomato processing affects the lycopene content [85]. Moreover, dietary factors and processing are reported to modu- late the bioavailability of lycopene [86]. Hence, there is scope for the development of novel dietary supplements to maximize the bioavailability of phyto- chemicals such as lycopene while also seeking to understand its functional role in health and disease [85].

Coronary Heart Diseases

Coronary heart disease (CHD) is one of the primary causes of death in the Western world. The emphasis of research so far has been on the relationship between serum cholesterol levels and the risk of CHD. In the industrialized world, cardiovascular disorders (CVD) are responsible for one of every three deaths in both men and women. Gorinstein et al. (1994) considered higher level of total cholesterol, LDL cholesterol (LDL-C), triglyc- erides, apolipoproteins B and C-III, and a reduced level of high density lipoprotein cholesterol (HDL-C), and apolipoproteins A-I as major risk factors (Gorinstein et al., 1998). Oxidation of LDL-C particles (Witzum and Steinberg, 1991; Aviram, 1993) results in accumulation of lipids into arterial wall resulting in onset of atherosclerosis (Steinbrecher et al., 1990; Gorinstein et al., 2000). Diets especially fruits and vegetables are the natu- ral sources of nutritional antioxidants thus preventing LDL ox- idation [86].

The evidence in support of the role of lycopene in the prevention of CHD is based on epidemiological observations of normal and at-risk populations. The most impressive population-based evidence comes from a multi-center case-control study (the EU- RAMIC study). According to this study, subjects from 10 Euro- pean countries were evaluated for a relationship between their antioxidant status and acute myocardial infarctions. By providing different dietary variables, only lycopene levels were found to be protective. These results were also confirmed by another Rotterdam Study [87].

Serum lycopene concentration plays a vital role in the early stages of atherosclerosis. Increased thickness of intima-media (the innermost lining of a blood vessel) has been shown to predict coronary events. A low serum lycopene concentration in Eastern Finland associated with an increased thickness of the intima-media. Recently, a prospective case-control study was conducted by Harvard University researchers on 39,876 women. According to them higher plasma lycopene concentrations are associated with a lower risk of cardiovascular disease in middle-aged and elderly women. Moreover, the possible in- verse associations with cardiovascular disease for higher levels of tomato-based products suggest that dietary lycopene or other phytochemicals consumed as oil-based or oil-containing tomato products confer cardiovascular benefits [88].

Cancer Insurgence

Sengupta in 2002 suggested that the consumption of garlic and tomato can reduce the damaging effect of carcinogenic. They also reported that different constitutes of garlic and tomato can be protected chromosomal aberrations especially lycopene have ability to protect the cell against oxidative damage. So tomato and tomato products not only reduce the risk of cardiovascular diseases but also cure cancer insurgence [89].

Epidemiology data indicated that reduction of prostate cancer in men was observed those who consume tomato and tomato- based products. In the Health Professionals Follow-Up Study, intake tomato products in week resulted in a lower risk of prostate cancer (Giovannucci 2002). It also has been reported that intake of tomato compound may lower down prostate cancer while caroteniods fraction are not related to prostate risk [90]. Lycopene is dominant antioxidant has been found to be very active in suppressing the certain cancer cell in humans. Lycopene causes an increase in in- tercellular communications, increased differential, and change the phosphorylation of regulatory proteins and act as antitumero- genic effect [91]. A comprehensive review of the epidemiological literature on the relation of tomato con- sumption and cancer was published by Giovannucci (1999). He found that among 72 studies, 57 reported inverse associations between tomato intake or blood lycopene level and the risk of cancer at a defined anatomic site. Thirty-five out of 57 of these inverse associations were statistically significant. A recently published meta-analysis by Etminan et al. (2004) formulated the assumption that intake of tomato-based products reduces the risk of prostate cancer. It was also observed that the prevention was slightly stronger for high intakes of cooked tomato products than raw tomatoes due to the bioavailability of lycopene, which is increased with processing, heat, and presence of fat [89,91].

Conclusions

Tomatoes are vegetables/fruits that contain significant amounts of dietary nutrients, including dietary fiber, reducing sugars, vitamins, minerals, protein, essential fatty acids, phytosterols and carotenoids. The nutritive elements play an important role in bodily func- tion and are beneficial in ameliorating chronic diseases. Tomatoes are also rich with health promoting bioactive phytochemicals, such as phenolic compounds including lycopene, quercetin, kaempferol, naringenin, caffeic acid and lutein. The bioactive constituents show antioxidant, antiproliferative, antidiabetic, anti-inflammatory, and other health-promoting activities, indicating the vast potential of tomato in preventing and/or ameliorating several chronic degenerative diseases. Lycopene and β-carotene are two main active ingredients in tomato that have strong antioxidant properties, which are linked with many health benefits, including cancer and heart diseases. They also participate in preventing the development of cataracts. Additionally, the water content and dietary fibers help the body in terms of hydration, bowel movements, reducing constipation, improving obesity through weight loss, and preventing colon cancer. All immune stimulating activities of tomatoes make them active ingredients for the development of functional foods. Thus, tomato is an excellent source of dietary nutrients and is useful in disease prevention.

Fruits and vegetables are gaining immense importance in the domain of nutrition owing to presence of vital phytochemicals and bioactive molecules. Their health promoting potentials are due to presence of functional ingredients, e.g., polyphenols, flavonoids, tannins, and anthocyanins. These compounds trigger and alter body metabolism and modulate detoxification mechanism. Thereby, provide protection against lifestyle disor- ders and cancer insurgence. Concluded that moderate amounts of whole food-based supplementation (2–4 servings) of tomato soup, tomato puree, tomato paste, tomato juice, or other tomato beverages, consumed with dietary fats, such as olive oil or av- ocados, leads to increases in plasma carotenoids, particularly lycopene. These foods may have both chemopreventive as well as chemotherapeutic values. In the light of recent clinical trials, a combination of naturally occurring carotenoids, including lycopene, in food sources and supplements, is a better approach to disease prevention and therapy, versus a single nutrient. However, until further research establishes significant health benefits of lycopene supplementation in humans, the conclusion may be drawn that consumption of naturally occurring carotenoid-rich fruits and vegetables, particularly processed tomato products containing lycopene, should be encouraged, with positive implications in health and disease.

References

[1]. Ahn, H., Hojin, M., Sunyoung, K., Ralph, L. and Kodell. (2002). A Newton- based approach for attributing tumor lethality in animal carcinogenicity stud- ies. Comput. Stat. Data. An. 3(38):263–283.

[2]. Alshatwia, A. A., Al Obaaida, Manal A., Al Sedairya, Sahar A., Al-Assaf, Abdullah H., Zhangb, J. J. and Leib, Kai Y. (2010). Tomato powder is more protective than lycopene supplement against lipid peroxidation in rats. Nutr. Res. 30:66–73.

[3]. Armstrong, G. A. and Hearst, J. E. (1996). Carotenoids 2: Genetics and molec- ular biology of carotenoid pigment biosynthesis. FASEB J. 10(2):228–37.

[4]. Aviram, M. (1993). Modified forms of low density lipoprotein and atheroscle- rosis. Ather. 1(4):1–9.

[5]. A-Young, L., Thomas, R., Kimball, S., Daniels, R.., Debra A., Philip R., Susan, M., Eichelberger, L. and Dolan, M. (1998). Nocturnal blood pressure in young patients with insulin-dependent diabetes mellitus: Correlation with cardiac function. J. Ped. 133(1):46–50.

[6]. A-Young, K., Yong-Jin, J., Yong, B.P., Mi-Kyung, L., Seon-Min, J., R0bin, A.M., Myung-Sook, C. (2012). Dose dependent effects of lycopene enriched tomato-wine on liver and adipose tissue in high-fat diet fed rats. Food Chem- istry. 130(1):42–48.

[7]. Badimon, L., Vilahur, G. and Padro, T. (2010). Nutraceuticals and atheroscle- rosis: human trials. Cardiovasc. Ther. 28(4):202–215.

[8]. Bankson, D. D., Countryman, C. J. and Collins, S. J. (1991). Potentiation of the retinoic acid-induced differantiation of HL-60 cells by lycopen. Am. J. Clin. Nutr. 53(Suppl):13.

[9]. Burns, J., Paul, D., Fraser, P. and Bramley, M. (2003). Identification and quantifi- cation of carotenoids, tocopherols and chlorophylls in commonly consumed fruits and vegetables. Phytochem. 62:939–947.

[10]. Butt, M. S., Nazir, A., Sultan, M. T. and Schroe¨n, K. (2008). Morus alba L. Nature's functional tonic. Trends in Food Sci. Technol. 19:505–512.

[11]. Calle, E. E., Thun, M. J., Petrelli, J. M., Rodriguez, C. and Heath, C. W. (1999). Body-mass index and mortality in a prospective cohort of US adults. NEJM. 341(15):1097–1105.

[12]. Cummings, D. E. and Schwartz, M. W. (2003). Genetics and pathophysiology of human obesity. Annu. Rev. Med. 54:453–471.

[13]. Etminan, M., Takkouche, B. and Caamano-Isorna, F. (2004). The role of tomato products and lycopene in the prevention of prostate cancer: A meta- analysis of observational studies. Cancer Epidemiol. Biomarkers Prev. 13(3): 340–345.

[14]. Ferreira, A. L. A., Salvadori, D. M. F., Nascimento, M. C. M., Rocha, N. S., Camila, R. C., Pereira, E. J., L. S., Matsubara, B. and Marcelo, S. P. L. (2007). Tomato-oleoresin supplement prevents doxorubicin-induced cardiac myocyte oxidative DNA damage in rats. Mutat. Res. 631:26–35.

[15]. Fraser, P. D., Truesdale, M. R., Bird, C. R., Schuch, W. and Bramley, P. M. (1994). Carotenoid biosynthesis during tomato fruit development' evidence for tissue-specific gene expression. Plant Physiol. 105:405–413.

[16]. Friedman, M., William, S., Breall, M., Barton, J., Sparagon, G. and Nancy, F. (1996). Effect of type A behavioral counseling on frequency of episodes of silent myocardial ischemia in coronary patients. Am. Heart J. 132 (5):933–937.

[17]. Fuhrman, B., Elis, A. and Aviram, M. (1997). Hypocholesterolemic effect of lycopene and beta-carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. Biochem. Biophys. Res. Commun. 233(3):658–662.
[18]. Giovannucci, E. (2002). Modifiable risk factors for colon cancer. Gastroenterol. Clin. N. 4(31):925–943.
[19]. Giovannucci, E. (1999). Tomatoes, tomato-based products, lycopene, and can- cer: Review of the epidemiologic literature. J. Natl. Cancer Inst. 91:317–331. Giovannucci, E., Ascherio, A., Rimm, E. B., Stampfer, M. J., Colditz, G. A. and Willett, W. C. (1995). Intake of carotenoids and retinol in relation to risk ofprostate cancer. J. Natl. Cancer Inst (Bethesda). 87:1767–76.
[20]. Goleniowski, M. E., Bongiovanni, G. A., Bongiovanni, L., Palacio, C. O. and Cantero, J. J. (2006). Medicinal plants from the “Sierra de Comechingones”, Arg. J. Ethnopharmacol. 107:324–341.
[21]. Gorinstein, S., Marina, Z., Moshe, W., Shmuel, H., Olga, Martin-B. and Simon,T. (1998). The influence of alcohol-containing and alcohol-free beverages on lipid levels and lipid peroxides in serum of rats. J. Nutritional Biochem. 9(12):682–686.
[22]. Salehi, B.; Sharifi-Rad, R.; Sharopov, F.; Namiesnik, J.; Roointan, A.; Kamle, M.; Kumar, P.; Martins, N.; Sharifi-Rad, J. Benefi- cial effects and potential risks of tomato consumption for human health: An overview. Nutrition 2019, 62, 201–208. [CrossRef] [PubMed]
[23]. Lenucci, M.S.; Cadinu, D.; Taurino, M.; Piro, G.; Dalessandro, G. Antioxidant composition in cherry and high-pigment tomato cultivars. J. Agric. Food Chem. 2006, 54, 2606–2613.
[24]. Elbadrawy, E.; Sello, A. Evaluation of nutritional value and antioxidant activity of tomato peel extracts. Arab. J. Chem. 2016,
[25]. Abdullahi, I.I.; Abdullahi, N.; Abdu, A.M.; Ibrahim, A.S. Proximate, Mineral and Vitamin Analysis of Fresh and Canned Tomato.Biosci. Biotechnol. Res. Asia 2016, 13, 1163–1169. [CrossRef]
[26]. Ramos-Bueno, R.P.; Romero-Gonzalez, R.; Gonzalez-Fernandes, M.J.; Guil-Guerrero, J.L. Phytochemical composition and in vitro anti-tumour activities of selected tomato varieties. J. Sci. Food Agric. 2017, 97, 488–496. [CrossRef]
[27]. Chaudhary, P.; Sharma, A.; Singh, B.; Nagpal, A.K. Bioactivities of phytochemicals present in tomato. J. Food Sci. Technol. 2018,
[28]. Campestrini, L.H.; Melo, P.S.; Peres, L.E.P.; Calhelha, R.C.; Ferreira, I.C.; De Alencar, S.M. A new variety of purple tomato as a rich source of bioactive carotenoids and its potential health benefits. Heliyon 2019, 5, e02831.
[29]. Vats, S.; Bansal, R.; Rana, N.; Kumawat, S.; Bhatt, V.; Jadhav, P.; Kale, V.; Sathe, A.; Sonah, H.; Jugdaohsingh, R.; et al. Unexplored nutritive potential of tomato to combat global malnutrition. Crit. Rev. Food Sci. Nutr. 2020, 1–32. [CrossRef]
[30]. Cheng, H.M.; Koutsidis, G.; Lodge, J.K.; Ashor, A.W.; Siervo, M.; Lara, J. Lycopene and tomato and risk of cardiovascular diseases: A systematic review and meta-analysis of epidemiological evidence. Crit. Rev. Food Sci. Nutr. 2019, 59, 141–158. [CrossRef]
[31]. Li, N.; Wu, X.; Zhuang, W.; Xia, L.; Chen, Y.; Wu, C.; Rao, Z.; Du, L.; Zhao, R.; Yi, M.; et al. Tomato and lycopene and multiple health outcomes: Umbrella review. Food Chem. 2020, 128396. [CrossRef]
[32]. Park, H.-A.; Hayden, M.M.; Bannerman, S.; Jansen, J.; Crowe-White, K.M. Anti-apoptotic effects of carotenoids in neurodegenera- tion. Molecules 2020, 25, 3453. [CrossRef] [PubMed]
[33]. Agarwal, S.; Rao, A.V. Tomato lycopene and its role in human health and chronic diseases. Can. Med. Assoc. J. 2000, 163, 739–744.
[34]. Navarro-González, I.; García-Alonso, J.; Periago, M.J. Bioactive compounds of tomato: Cancer chemopreventive effects and influence on the transcriptome in hepatocytes. J. Funct. Foods 2018, 42, 271–280. [CrossRef]
[35]. Hossen, M.S.; Ali, M.Y.; Jahurul, M.H.A.; Abdel-Daim, M.M.; Gan, A.H.; Khalil, M.I. Beneficial roles of honey polyphenols against some human degenerative diseases: A review. Pharmacol. Rep. 2017, 69, 1194–1205. [CrossRef]
[36]. Zhu, R.; Chen, B.; Bai, Y.; Miao, T.; Rui, L.; Zhang, H.; Xia, B.; Li, Y.; Gao, S.; Wang, X.-D.; et al. Lycopene in protection against obesity and diabetes: A mechanistic review. Pharmacol. Res. 2020, 159, 104966. [CrossRef]
[37]. Sakemi, Y.; Sato, K.; Hara, K.; Honda, M.; Shindo, K. Biological Activities of Z-Lycopenes Contained in Food. J. Oleo Sci. 2020,
[38]. Saini, R.K.; Rengasamy, K.R.; Mahomoodally, F.M.; Keum, Y.-S. Protective effects of lycopene in cancer, cardiovascular, and neu- rodegenerative diseases: An update on epidemiological and mechanistic perspectives. Pharmacol. Res. 2020, 155, 104730. [CrossRef]
[39]. Imran, M.; Ghorat, F.; Ul-Haq, I.; Ur-Rehman, H.; Aslam, F.; Heydari, M.; Shariati, M.A.; Okuskhanova, E.; Yessimbekov, Z.; Thiruvengadam, M.; et al. Lycopene as a natural antioxidant used to prevent human health disorders. Antioxidants 2020, 9, 706. [CrossRef]
[40]. Tohge, T.; Fernie, A.R. Metabolomics-inspired insight into developmental, environmental and genetic aspects of tomato fruit chemical composition and quality. Plant Cell Physiol. 2015, 56, 1681–1696. [CrossRef]
[41]. Claye, S.S.; Idouraine, A.; Weber, C.W. Extraction and fractionation of insoluble fiber from five fiber sources. Food Chem. 1996,57, 305–310. [CrossRef]
[42]. Delzenne, N.M.; Olivares, M.; Neyrinck, A.M.; Beaumont, M.; Larsen, T.M.; Benitez-Paez, A.; Romani-Perez, M.; Garcia-Campayo, V.; Bosscher, D.; Sanz, Y.; et al. Nutritional interest of dietary fiber and prebiotics in obesity: Lessons from the MyNewGut consortium. Clin. Nutr. 2020, 39, 414–424. [CrossRef] [PubMed]
[43]. Merenkova, S.; Zinina, O.; Stuart, M.; Okuskhanova, E.; Androsova, N. Effects of dietary fiber on human health: A review.
[44]. Человек. Спорт. Медицина 2020, 20, 106–113. [CrossRef]
[45]. Gorinstein, S., Oates, C. G., Chang, S. M., and Lii, C. Y. (1994). Enzymatic hydrolysis of sago starch. Food Chemistry. 49(4):411–417.
[46]. Gorinstein, S. W., Kulasek, G., Elzbieta, B., Maria, L., Marina, Z., Marek M. and Simon, T. (2000). The effects of diets, supplemented with either whole persimmon or phenol-free persimmon, on rats fed cholesterol. Food Chem. 3(70):303–308.
[47]. Gu, Y., Ajay, S., Sharmila, B. and Neena, S. (2008). Pathogenic mutations in the glycosylphosphatidylinositol signal peptide of PrP modulate its topology in neuroblastoma cells. Mol. Celluar Neurosci. 4(37):647–656.

[48]. Hadley, C. W., Miller, E. C., Schwartz, S. J. and Clinton, S. K. (2002). Toma- toes, lycopene, and prostate cancer: Progress and promise. Exp. Biol. Med (Maywood). 227(10):869–880.

[49]. Hsu, Y., Lai, C., Chang, C., Fan, C., Chen, C. and Wu, C. (2008). Characterizing the lipidlowering effects and antioxidant mechanisms of tomato paste. Biosci. Biotechnol. Biochem. 72(3):677–685.

[50]. Ibrahim, H. S., Ahmed, L. A. and El-din, M. M. E. (2008). The functional role of some tomato products on lipid profile and liver function in adult rats. J. Med. Food. 11(3):551–559.

[51]. Khachik, F., Beecher, G. R., Goli, M. B. and Lusby, W. R. (1991). Separation, identification, and quantification of carotenoids in fruits, vegetables and hu- man plasma by high performance liquid chromatography. Pure Appl. Chem. 63:71–80.

[52]. Khachik, F., Beecher, G. R., Goli, M. B. and Lusby, W. R. (1992a). Separa- tion and quantification of carotenoids in foods. In: Methods in Enzymology. Packer, L. Ed., New York: Academic Press, 213:347–359.

[53]. Khachik, F., Goli, M. B., Beecher, G. R., Holden, J., Lusby, W. R., Tenorio,

[54]. M. D. and Barrera, M. R. (1992b). The effect of food preparation on qualitative and quantitative distribution of major carotenoid constituents of tomatoes and several green vegetables. J. Agric. Food Chem. 40:390–398.

[55]. Khachik, F., Carvalho, L., Bernstein, P. S., Garth, J., Muir, D. Z. and Katz, N. B. (2002). Chemistry, distribution, and metabolism of tomato carotenoids and their impact on human health. Exp. Biol. Med. 227:845–851.

[56]. Kim, H., Lee, K., Park, Y. B., Jeon, S. and Choi, M. (2008). Dietary docosa- hexaenoic acidrich diacylglycerols ameliorate hepatic steatosis and alter hep- atic gene expressions in C57BL/6J-Lep(ob/ob) mice. Mol. Nutr. Food Res. 52(8):965–973.

[57]. Klipstein-Grobusch, K., Launer, L. J., Geleijnse, J. M., Hofman, A. and Witte- man, J. C. M. (2000). Serum carotenoids and atherosclerosis: The Rotterdam Study. Ather. 1(148):49–56.

[58]. La Vecchia, C. (2002). Tomatoes, lycopene intake, and digestive tract and female hormone-related neoplasms. Exp. Biol. Med (Maywood). 227(10):860–863.

[59]. Lee, S. K., Jung, H. L., Hye, H. Y., Dong, H. K., Yurngdong, J. and Tae, C. J. (2006). Characterization of human liver cytochrome P450 enzymes involved in the metabolism of rutaecarpine. J. Phar.Biom. An. 1(41):304–309.

[60]. Lindshield, B. L., Canene-Adams, K. and Erdman, J. W. (2007). Ly- copenoids: Are lycopene metabolites bioactive? Arch. Biochem. Biophys. 458(2):136–140.

[61]. Liyanapathirana, C. M. and Shahidi, F. (2004). Antioxidant activity of wheat extracts as affected by in vitro digestion. Biofactors. 21:325–328.

[62]. Manach, C., Scalbert, A., Morand, C., Re´me´sy, C. and Jime´nez, L. (2004). Polyphenols: Food sources and bioavailability. Americ. J. Clin. Nutri. 79:727–747.

[63]. Markovits, N., Ben Amotz, A. and Levy, Y. (2009). The effect of tomato- derived lycopene on low carotenoids and enhanced systemic inflammation and oxidation in severe obesity. IMAJ. 11(10):598–601.

[64]. Paetau, I., Khachik, F., Brown, E. D., Beecher, G. R., Kramer, T. R., Chittams,

[65]. J. and Clevidence, B. A. (1998). Chronic ingestion of lycopene-rich tomato juice or lycopene supplements significantly increases plasma concentrations of lycopene and related tomato carotenoids in humans. Am. J. Clin. Nutr. 68:1187–1195.

[66]. Park, K., Antonio, F. and Kwang, Si, C. (2006). Application of enzyme-linked immunosorbent assay (ELISA) for the study of reproduction in the Manila clam Ruditapes philippinarum (Mollusca: Bivalvia): II. Impacts of Perkinsus olseni on clam reproduction. Aqua. 251(2–4):182–191.

[67]. Agarwal S, Rao AV (2000) Tomato lycopene and its role in humanhealth and chronic diseases. Can Med Assoc J 163(6):739–744

[68]. Amir H, Karas M, Giat J, Danilenko M, Levy R, Yermiahu T, SharoniY (1999) Lycopene and 1, 25-dihydroxyvitamin d3 cooperate inthe inhibition of cell cycle progression and induction ofdifferentiation in hl-60 leukemic cells. Nutr Cancer33(1):105–112.

[69]. Bae JW, Bae JS (2011) Barrier protective effects of lycopene inhuman endothelial cells. Inflamm Res 60(8):751–758

[70]. Bai SK, Lee SJ, Na HJ, Ha KS, Han JA, Lee H, Kim YM (2005)[beta]-carotene inhibits inflammatory gene expression in lipopolysaccharide-stimulated macrophages by suppressingredox-based NF-[kappa] B activation. Exp Mol Med 37(4):323

[71]. Burgess LC, Rice E, Fischer T, Seekins JR, Burgess TP, Sticka SJ,Klatt K (2008) Lycopene has limited effect on cell proliferationin only two of seven human cell lines (both cancerous andnoncancerous) in an in vitro system with doses across thephysiological range. Toxicol In Vitro 22(5):1297–1300.

[72]. Ezekiel R, Singh N, Sharma S, Kaur A (2013) Beneficial phytochemicals in potato—a review. Food Res Int 50(2):487–496.

[73]. FAOSTAT (2014) Global tomato production. http://faostat.fao.org/.Accessed on June–JulyFeng D, Ling WH, Duan RD (2010) Lycopene suppresses LPSinduced NO and IL-6 production by inhibiting the activation ofERK, p38MAPK, and NF-jB in macrophages. Inflamm Res59(2):115–121.

[74]. Park, K., Antonio, F. and Kwang, Si, C. (2006). Application of enzyme-linked immunosorbent assay (ELISA) for the study of reproduction in the Manila clam Ruditapes philippinarum (Mollusca: Bivalvia): II. Impacts of Perkinsus olseni on clam reproduction. Aqua. 251(2–4):182–191.

[75]. Pellegrini, N., Riso, P. and Porrini, M. (2000). Tomato consumption does not affect the total antioxidant capacity of plasma. Nutr. 16:268– 271.

[76]. Sengupta, A., Ghosh, S. and Sukta, D. (2002). Administration of garlic and tomato can protect from carcinogen induced clastogenicity. Nutr. Res. 7(22):859–866.

[77]. Sesso, H. D., Buring, J. E., Norkus, E. P. and Gaziano, J. M. (2004). Plasma lycopene, other carotenoids, and retinol and the risk of cardiovascular disease in women. Am. J. Clin. Nutr. 79(1):47–53.

[78]. Shi, J. and Le Maguer, M. (2000). Lycopene in tomatoes: Chemical and physical properties affected by food processing. Crit. Rev. Food Sci. Technol. 40: 1–42.

[79]. Story, E. N., Kopec, R. E., Schwartz, S. J. and Harris, G. K. (2010). An update on the health effects of tomato lycopene. Annu. Rev. Food Sci. Technol. 1(1):189–210.

[80]. Veeramachaneni, S., Ausman, L. M., Choi, S. W., Russell, R. M. and Wang,

[81]. X. (2008). High dose lycopene supplementation increases hepatic cy- tochrome P4502E1 protein and

inflammation in alcohol-fed rats. J. Nutr. 138(7):1329–1335.

[82]. Walfisch, Y., Walfisch, S., Agbaria, R., Levy, J. and Sharoni, Y. (2003). Lycopene in serum, skin and adipose tissues after tomato-oleoresin supplementation in patients undergoing haemorrhoidectomy or peri-anal fistulotomy. Br. J. Nutr. 90(4):759–766.

[83]. Willcox, J. K., Catignani, G. L. and Lazarus, S. (2003). Tomatoes and cardio- vascular health. Crit. Rev. Food Sci. Technol. 43:1–18.

[84]. Zeb, A. and Mehmood, S. (2004). Carotenoids contents from various sources and their potential health applications. Pak. J. Nutr. 3:199–204.

[85]. Zhang, L. X., Cooney, R. V. and Bertram, J. S. (1992). Carotenoids up-regulate connexin43 gene expression independent of their provitamin A or antioxidant properties. Cancer Res. 52:5707–12.

[86]. Ziegler, R. G. (1991). Vegetables, fruits and carotenoids and the risk of cancer.Am. J. Clin. Nutr. 53(Suppl):251–259.

[87]. Ziegler, R. G., Mayne, S. T. and Swanson, C. A. (1996). Nutrition and lung cancer. Cancer Causes Control. 7:157–177.

[88]. Manach, C., Scalbert, A., Morand, C., Re´me´sy, C. and Jime´nez, L. (2004). Polyphenols: Food sources and bioavailability. Americ. J. Clin. Nutri. 79:727–747.

[89]. Markovits, N., Ben Amotz, A. and Levy, Y. (2009). The effect of tomato- derived lycopene on low carotenoids and enhanced systemic inflammation and oxidation in severe obesity. IMAJ. 11(10):598–601.

[90]. Paetau, I., Khachik, F., Brown, E. D., Beecher, G. R., Kramer, T. R., Chittams,J. and Clevidence, B. A. (1998). Chronic ingestion of lycopene-rich tomato juice or lycopene supplements significantly increases plasma concentrations of lycopene and related tomato carotenoids in humans. Am. J. Clin. Nutr. 68:1187–1195.

[91]. Park, K., Antonio, F. and Kwang, Si, C. (2006). Application of enzyme-linked immunosorbent assay (ELISA) for the study of reproduction in the Manila clam Ruditapes philippinarum (Mollusca: Bivalvia): II. Impacts of Perkinsus olseni on clam reproduction. Aqua. 251(2–4):182–191.