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# Phytochemical and Nutritional Profiling of Tomatoes; Impact of Processing on Bioavailability - A Comprehensive Review

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## ABSTRACT

Tomatoes (*Solanum lycopersicum*) are of great significance in terms of the worldwide consumption of nutritional diets. More than half of the production is sold as fresh products, while the whole fruit is still typically processed into various products, including canned tomatoes, paste, juice, and puree. Tomatoes are rich in phenolic compounds, which are generally present as soluble and bound forms in nature. Large amounts of nutritional and bioactive compounds such as phenolics, flavonoids, carotenoids, vitamins, minerals and glycoalkaloids have drawn increasing interest in tomato fruits. However, there appears to be a certain anti-nutritional compound that negatively influences human health. As the role of antioxidants in human nutrition has gained increased interest, the bioavailability of tomato fruits is of great importance to be researched and studied, especially due to their associated health benefits for a number of chronic diseases, including certain types of cancer and cardiovascular disease. Nevertheless, the processing of tomatoes into various end products, including mechanical and heat treatments, is considered to be one of the most significant factors that are potentially affected by those nutritional properties, anti-nutritional compounds and causing changes in the bioavailability of antioxidants. In this review, the nutritional and anti-nutritional compounds, and related health and side effects were discussed. The review also focused on the effects of different food processing techniques on the *in vivo* and *in vitro* bioavailability of tomato antioxidants.

## KEYWORDS

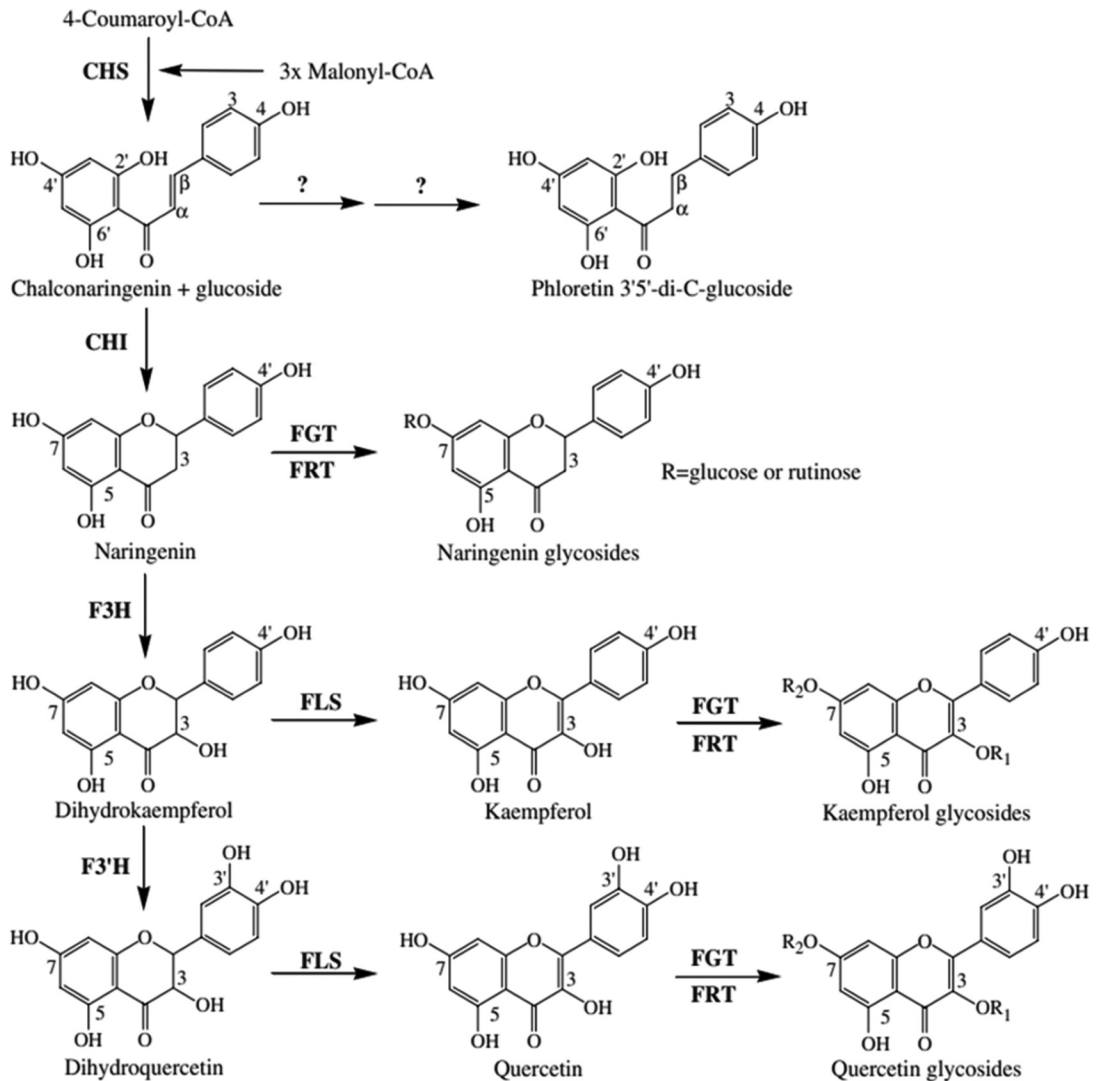
Tomato; bioactive compounds; bioavailability; processing effects; health properties

## Introduction

Tomatoes (*Solanum*), which are typically red fruits, belong to the Solanaceae family. The cultivated fruits generally have 1–3 meters in height planted in temperate, subtropical, and tropical areas. The stem of tomato fruits is weak and usually spread from the ground and other plants.<sup>[1]</sup> It can be seen from the image (Fig. 1) that the tomato peel can be divided into three parts, including peel, red layer

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**Figure 1.** Biosynthetic pathway to flavonoids in tomato.

and pericarp thickness.<sup>[2]</sup> The exocarp, which is also known as the peel, is composed of a cuticle layer, a single layer of epidermal cells, and two to four layers of hypodermal cells with unevenly thickened walls.<sup>[3]</sup> While the mesocarp, which is the red layer, was composed of parenchymal cells, the sizes of the cells in the mesocarp were much larger than those in the exocarp. Tomato peel normally refers to the residue of tomatoes following various processing regimes and mainly consists of peels and seeds.

The origin of tomatoes consumption is rather controversial.<sup>[4]</sup> Blanca, et al. reported that the center of the coastal area of Peru desert is the original place, while other studies indicated the dual center which is located in the coastal region between the Andes and the ocean, and the area from southern Mexico to Guatemala.<sup>[5]</sup> Since the domestication of tomato fruits, their appearance and size have also undergone a great number of changes.<sup>[6]</sup> Although tomatoes have a variety of species in a taxonomy, they share almost the same traits. Moreover, domesticated species are not only larger than wild tomatoes, but the fruits also have tremendous shape variation due to domestication. The majority of cultivated tomatoes are formed generally in a round shape, while domesticated tomatoes can be found in other shapes.<sup>[6]</sup>

Tomatoes (*Solanum lycopersicum*) are important parts of processed vegetable crops. The total tomato production in the global market has increased about fivefold, from 27.6 million tons in 1961 to 171 million tons in 2014.<sup>[7]</sup> For Australia, tomato production values the second greatest position after potatoes, worth 674.2 million AUD in 2019.<sup>[8]</sup> However, similarly to other fruits and vegetables, tomatoes are prone to be injured and spoilage during processing, storage, or transportation, making rapid consuming or better preserving methods necessary.

There are almost half of the fresh tomatoes prepared for the processing industries are likely to generate food waste. Nutritionally valued byproducts from tomato processing are mainly divided into 3 parts, including peel, seeds and pulp (Fig. 1), that could be utilized to produce other forms of products, such as tomato soup, puree, ketchup, or paste.<sup>[9,10]</sup> In the whole supply chain, 53% of total production is available for a fresh supply like the food service industry, and household consumption, while others are utilized for processing (47%) and export (<1%). When it comes to the nutritional values, the major bioactive compounds in tomatoes are phenolics, carotenoids, and vitamins, which contain various physiological benefits, such as anti-inflammation, antimicrobial, vasodilatory, and cardio-protective.<sup>[9,11]</sup> There is a wide range of nutrients present in tomatoes that are beneficial for health and widely utilized in various diets (Table 1). From most of the macro-nutrients, the low amount of fat content and cholesterol makes individuals the beneficiary of tomato fruits.

Apart from that, carbohydrates and dietary fiber represent the most of macro nutritional compounds, along with proteins and amino acids. As for the micro-nutrients, the concentration of vitamins and minerals like Vitamin A, ascorbic acid, and potassium are relatively high in tomatoes. It has been suggested by<sup>[15]</sup>Canene-Adams, et al. that a weight of 100 g tomatoes are able to provide 900 UE of vitamin A, 82.5 mg of vitamin C, and 3500 mg of potassium. The appearance of other bioactive compounds that showed various benefits to human health, such as carotenoids, and polyphenols, also showed a significant amount.<sup>[16]</sup> The concentration variability of tomato nutrients relies on various factors, including genetic differences, growing conditions, temperature, irradiance, humidity, and salinity.<sup>[17]</sup> The color of tomato fruits determines the maturity of the fruits, and the ratio of starch and high soluble solids which predominately are glucose and fructose in commercial tomatoes. This depends on the sugar metabolism process, which will be impacted by cultivars and their substantial characteristics. Specifically, there appears to be a small amount of starch stored in green

**Table 1.** Nutrients present in different types of tomatoes with different conditions, colors and maturity levels.

Nutrients (Units)	Red raw tomatoes (per 100	Red cooked tomatoes (per 100	Green raw tomatoes (per 100	References
	g)	g)	g)	
Water (%)	94.5	94.34	93	[12–14]
Protein (g)	0.88	0.96	1.2	
Carbohydrate (g)	3.92	4.01	5.2	
Total dietary fibre (g)	1.2	0.7	1.1	
Total lipids(g)	0.2	0.11	0.2	
Minerals (mg) -				
Calcium (Ca)	10	11	13	
Magnesium (Mg)	11	9	10	
Phosphorus (P)	24	28	28	
Potassium (K)	237	218	204	
Sodium (Na)	5	11	13	
Zinc (Zn)	0.17	0.14	0.07	
Manganese (Mn)	0.114	0.105	0.101	
Vitamins (mg) -				
Vitamin E	0.54	0.56	0.38	
Vitamin C	12.7	22.8	23.5	
Thiamin	0.037	0.036	0.06	
Vitamin B-6	0.06	0.079	0.081	
Niacin	0.594	0.532	0.5	
Riboflavin	0.019	0.022	0.04	
Lycopene (mg)	20.54	31.63	0	

tomatoes, followed by reaching the highest level with maturity.<sup>[17]</sup> Then, starch is about to be hydrolyzed when the fruits reach the highest maturity level.<sup>[18]</sup> The fundamental objective of this review was to summarize the comprehensive overview of nutritional and bioactive compounds and the impact of the processing bioavailability of tomatoes. Additionally, the health benefits of bioactive phytochemicals in tomatoes are also highlighted in this review.

## Bioactive compounds in tomato

### Phenolics

Fruits, vegetable, and their by-products are rich in phenolic compounds, which belong to phytochemicals that imply bioactivity. The main phenolics presented in raw tomatoes and commercial products can be classified into two general parts, including flavonoids, such as rutin, naringenin, kaempferol, quercetin, and phenolic acids. Among these, naringenin is a primer for more advanced flavonoid structures but also a substrate in glycosylation reactions.<sup>[19]</sup> Figure 1 illustrates the biosynthetic pathway of flavonoids in tomatoes.

There are a great number of phenolic compounds and flavonoids studied and found in tomato fruits. It can be seen that the concentration of the naringenin chalcone was regarded as the most abundant phenolic compound in tomatoes, which were 309.7 mg per 100 g dry weight. Then, 3-caffeoylquinic acid and quercetin-3-rutinoside showed the second and third most amounts in tomatoes, which were 71.7 mg per 100 g dry weight and 60 mg per 100 g dry weight, respectively.<sup>[20]</sup> When it comes to the detected flavonoids, the most abundant compound is rutin, followed by naringenin (0.65–1.19 mg per 100 g fresh weight), quercetin (0.048–0.141 mg per 100 g fresh weight) and myricetin (0.017–0.286 mg per 100 g fresh weight). Moreover, the most abundant phenolic acid compound found in tomatoes was chlorogenic acid, which occupied 0.75–1.38 mg per 100 g fresh weight.

Some factors are likely to influence the concentration and profile of phenolic compounds.<sup>[21]</sup> Firstly, tomato cultivars and variety are considered to be one of the main drivers of differentiating various phenolic contents. For instance, the phenolics found in cherry tomatoes were reported to be 440 mg per 100 g dry weight,<sup>[20]</sup> while other cultivars from the market and the wild contain 26.34–66.08 mg/100 g FW and 62.82–141.98 mg GAE/100 g fresh weight of gallic acid.<sup>[20]</sup> Second, different thermal or non-thermal processing steps will also impact the phenolics in tomatoes positively and negatively.<sup>[22]</sup> Martínez-Huélamo, et al. reported that the flavonoid contents of tomato by-products tend to improve after processing compared to the fresh materials. Among these, there observed a 7-fold for the flavanone naringenin content and a 4-fold increase in the protocatechuic acid and 3-caffeoylquinic acid. Additionally, the level of rutin was improved two times compared to fresh tomatoes, which is similar to another study that which the tomato sauce showed increased results in naringenin 20 times higher and antioxidant activity 1.2 times higher after processing.<sup>[23]</sup>

Moreover, the significant differences in the phenolic content and profile have been suggested in diverse parts of tomatoes, which include the peel, flesh, and seed. The research conducted by<sup>[24]</sup> Toor and Savage indicated that the skin and seeds of tomatoes contain a higher content of polyphenol than the flesh (12.7 mg GAE/100 g fresh weight), which were 29.1 and 22 respectively. Similarly, other results indicated that several other cultivars, such as grape, cherry, and bola types contain a higher phenolic content of 2.2 times than that in the peel and seeds.<sup>[25]</sup>

### Carotenoids

Carotenoids are responsible for natural pigmentation in fruits, vegetables, algae, and photosynthetic bacteria, which can be divided into two major groups. There are above 700 substances in this family which is characterized by a structure of linear polyisoprene with conjugated double-bonds. Among these, compounds in the xanthophyll group, such as lutein and zeaxanthin, are functional containing

oxygen, while  $\alpha$ -carotene,  $\beta$ -carotene and lycopene from the carotene group have only a parent hydrocarbon chain without functional properties.<sup>[26]</sup> Carotenoids are generally provided by vegetables or fruits, making tomatoes the main resource of this compound. Thus, tomatoes can be utilized as functional foods or ingredients in other types of products. The concentration of carotenoids in tomato products and the raw materials are documented in Table 2.<sup>[1]</sup>

There are several carotenoids discovered in tomato fruits. For instance, peels and other tomato by-products contain a high level of carotenoids, reaching up to about 88%.<sup>[1,9]</sup> Next,  $\beta$ -carotene, obtained in less than 1% of tomatoes, is mainly present in the tissues that are responsible for the photosynthesis processes of unmaturing green tomatoes. The other carotenoids also represented less than 1%.<sup>[38]</sup>

### Lycopene

Lycopene ( $\alpha$ -carotene), the most carotenoid group in tomatoes, is a bright red pigment carotenoid, indicating the maturity of fruits.<sup>[39,40]</sup> The lycopene content in tomatoes can be strongly impacted by various factors, including genetic as well as environmental factors.<sup>[41,42]</sup> In terms of the genetic aspect, fruit color is an accurate indicator of lycopene content, which red cultivars include more lycopene than the yellow cultivars, and orange cultivars show less content than the most red cultivars.<sup>[43]</sup> However, certain black tomatoes, namely Black Cream, display a higher level of lycopene than red cultivars.<sup>[44,45]</sup> In addition, different varieties of tomato make a difference in the lycopene content. For instance, among the three varieties of tomatoes, the content of lycopene in cherry tomatoes (48.9–116.7 mg/kg ww) is noted with a higher trend than that in the cluster (12.6–35 mg/kg ww) as well as round tomatoes (4.3–47 mg/kg ww).<sup>[44,46]</sup>

Except for genetic elements, environmental factors affect lycopene levels in tomatoes as well. Different intensities of sunlight will greatly affect the growth of plants, including tomato crops. One study showed that tomato crops treated with 25% black color produced higher levels of lycopene and beta-carotene compared to tomatoes treated with 40% red, yellow and pearl colors.<sup>[47]</sup> Moreover, the lycopene content of tomatoes grown in the greenhouse was found to be about 40% higher than that of tomatoes grown in the open field. For tomato crops cultivated in warm regions with high solar radiation, the effect of leaf shading on lycopene content may be more important.<sup>[48]</sup>

Temperature and humidity are other possible environmental factors that affect lycopene content in tomatoes. One study illustrated that tomato antioxidant content decreased when the temperature was above 32°C or below 12°C.<sup>[49]</sup> Lycopene content in tomatoes demonstrates a higher value at 15°C and 25°C than at 7°C.<sup>[50]</sup> Tomatoes grown at an average maximum air humidity of 73% and a maximum average temperature of about 40°C have lower lycopene levels.<sup>[48]</sup> Further, the lycopene content can be more easily impacted by the fruit surface temperature, which is a more accurate predictor of lycopene levels in fruit than the air temperature. The more the fruit is directly exposed to strong sunlight, the higher its surface temperature, causing the lycopene content to decrease.<sup>[48]</sup>

Proper water supply operations offer benefits including water and energy preservation, but they also impact yield quality. There are studies on the water supply effect on carotenoid composition as well as lycopene content in tomatoes.<sup>[51,52]</sup> According to<sup>[52]</sup> Takács, et al., 75% of crop evapotranspiration provided until the start of ripening was a balanced water supply level in terms of the lycopene content along with the yield.<sup>[52]</sup> In another study, lycopene content in tomato cultivar (Triple Red)

**Table 2.** Concentration of carotenoids in tomatoes and tomato-based food products (mg/100 g).

Carotenoids	Fresh fruit	Tomato paste	Tomato sauce	Tomato juice	Tomato soup	Tomato puree	Ref.
Lycopene	111.84 ± 0.99	107.00 ± 0.71	7.3–18.0	5.0–10.77	8.0–10.92	16.67	[1,27–37]
$\beta$ -carotene	5.64 ± 0.05	6.11 ± 0.14	0.45–12.8	0.18–0.56	0.23±0.047	0.41	
$\alpha$ -carotene	0.101	nd	nd	nd	nd	nd	
Phytofluene	0.39–0.82	3.63±0.38	1.27±0.2	0.83±0.14	0.72±0.176	1.08	
Phytoene	0.43–1.86	8.36±0.80	2.95±0.43	1.90±0.19	1.72±0.172	2.4	
Lutein	0.08–0.123	0.34±0.11	nd	0.06±0.02	0.09±0.02	0.09	

from 100% irrigated was noted significantly greater than that discovered in fruit with no irrigation.<sup>[51]</sup> Thus, to produce tomatoes with a high amount of bioactive nutrients, it is critical to optimize irrigation.

Fruit age is another significant factor affecting lycopene content in tomatoes. One study found that fruit harvested in June 2001 exhibited lower lycopene levels than fruit harvested after July. Measured lycopene in tomatoes harvested in September 2001 was lower than in fruits harvested in August.<sup>[48]</sup> Physiologically immature fruit contains less lycopene than fruit that is physiologically ripe, while physiologically overripe fruit generally has less lycopene.<sup>[53]</sup> The content of lycopene is influenced by the process of respiration, which happens during storage and causes lycopene to break down into terpenes, lowering the lycopene level.<sup>[54,55]</sup> Besides, there is a relationship between lycopene existence and the sugar content in tomatoes.<sup>[43]</sup> Coyago-Cruz, et al. reported that the unavailability of sucrose in nonmature fruits could directly contribute to the no detection of lycopene in some Spain varieties.

Fruit processing plays an important part in the lycopene content in tomatoes. For example,<sup>[14]</sup> Górecka, et al. reported that the lycopene content in ripened tomatoes was 1.9–6.5 mg per 100 g fresh weight. However, other tomato-based foods contain a higher level of lycopene concentration, which is 54 mg per 100 g in tomato concentrates, 16.6 mg per 100 g in ketchup and 20.86 mg per 100 g in sauces.<sup>[56]</sup>

### ***β-Carotene***

Carotenoids are recognized as the second most abundant carotenoid in tomatoes and their product is β-carotene, the content level is highly lower than lycopene, about 0.23–2.83 mg per 100 g of fresh weight.<sup>[57]</sup> It is also responsible for the yellow to orange pigmentation in fruits. From a structural perspective, the two retinyl groups in β-carotene make this compound show a pro-vitamin A activity.

### ***Minerals and vitamins***

Tomato is a significant source of micronutrients, including vitamins, such as vitamin A, B, and E, and minerals like K, Na, Mg, and S. In fresh tomatoes, the most abundant mineral is potassium, which contains 237 mg per unit, followed by phosphorus (24 mg), Magnesium (11 mg), and Sodium (5 mg). What is more, tomato wastes obtained from the processing industry are not only an excellent source of various phytochemicals but minerals as well.<sup>[58]</sup> Zhivkova determined potassium element showed the highest concentration level in wasted tomatoes, which was up to 2238 mg per unit, followed by S, Mg, and Na, which were 135, 134, and 132 mg/kg, respectively. Similarly, the study conducted by<sup>[59]</sup> Asquer, et al. also indicated that the highest mineral level (9.97 mg/kg) in wasted tomatoes was potassium.

Regarding vitamin C, tomato represents one of the main sources of this compound in various foods. As for its characteristics, it is water-soluble and ready to be stored in the body and be utilized for several biological functions.<sup>[60]</sup> In fresh tomatoes, the concentration of this vitamin varies from 8 to 16.3 mg per 100 g fresh weight. However, it is highly dependent on factors like the genotype, varieties, fruit development, as well as environmental conditions.<sup>[61]</sup> As one of the effective antioxidant compounds, vitamin C shows a great number of health-related effects. Regarding the vitamin E, it is a type of fat-soluble compound that is composed of different chemical structures, including four tocopherols (α-, β-, γ- and δ), and four tocotrienols (α-, β-, γ- and δ). The α-tocopherol is defined as the standard recommended dietary allowances of vitamin E, as it is the only form of vitamin E maintained in human plasma.<sup>[62]</sup> Therefore, vitamin E is of great importance in daily diet due to the lack of ability in the human body to synthesize this vitamin.<sup>[63]</sup> Consequently, tomato is of great importance to be consumed in daily diets as a great source of vitamin E.



## Proteins and amino acids

As an important part of fresh tomatoes, the practical value and recycling capability of tomato seeds cannot be underestimated. Aside from a higher content of bioactive compounds in tomato seeds, the crude protein was also reported to take up approximately 24.5% of the content and the glutamic acid and aspartic acid had the highest level.<sup>[64]</sup> Most proteins in tomato fruits are preserved in the seeds. Recent investigations have indicated that the content of proteins found in tomato seeds could be comparable to that of other plants, such as wheat for almost twice the percentage.<sup>[65]</sup> The specific protein content in tomato and tomato-based foods were reported to reach up to more than 21.9% per dry weight basis.<sup>[66]</sup> Moreover, proteins from tomatoes showed important health effects. For example, after an experiment on the golden Syrian male hamster, results showed that there was a cholesterol-lowering effect after consuming defatted tomato seeds, which were rich in protein content.<sup>[67]</sup>

Amino acids are of great significance in terms of the growth of organisms due to their diverse biological functions, including muscle protein metabolism regulation, growth and immunity control, adiposity reduction function, and promoting efficiency of food utilization.<sup>[68]</sup> In the protein of tomato seeds, the essential amino acids ratio was reported to be 39.5%.<sup>[69]</sup> Besides, the proportions of hydrophilic amino acids, which are consist of lysine, histidine, aspartic acid, glutamic acid and arginine, as well as the hydrophobic amino acids, including alanine, valine, leucine, isoleucine and phenylalanine, were presented in 41.6% and 26.4%. As mentioned before, a higher level of glutamate procurer glutamic acid contributes to the popularity of tomato seeds.<sup>[70]</sup>

## Carbohydrates

The main carbohydrates in tomatoes have two major parts, including soluble sugar content like glucose and fructose and the non-soluble dietary fibers. Also, due to the higher level of reducing sugar content, better sweetness and texture of final products make the industry a more successful market.<sup>[71]</sup> However, the content of carbohydrates in tomatoes and its related products tend to be effective in flavors and texture, as sugar metabolism appears to be controlled by several quantitative traits.<sup>[72]</sup> When it comes to dietary fiber, which contains a mixture of substances like cellulose, hemicelluloses, lignin, pectic, and gums, it has shown numerous benefits to the digestive tract. During different industrial processing stages, the average composition of neutral detergent fiber and total sugars in tomato pomace was 59.03% and 25.73%, respectively.<sup>[73]</sup> In contrast,<sup>[58]</sup> Zhivkova researched the total dietary fiber and sugar in tomato wastes and found that the nutrition ratio was only about 1.18% and 3.20%, while water content taken up to 94%. This significant difference is possible because of the experiment's material resources.

## Fatty acids

The fat content predominately exists in tomato peels and seeds. There are approximately 0.2 g/kg of total fat weight in fresh tomatoes, while the tomato pomace is rich in fat, containing about 12–18% in tomato seeds.<sup>[74]</sup> What is more, there is approximately 20% of oil content and the composition of fatty acids is similar to that of low linolenic soya bean oil.<sup>[75]</sup> As for the extraction of fats, about 75% to 85% of them can be easily extracted using a solvent. In tomato wastes, the most abundant fatty acids were reported to be unsaturated ones, which were 77.04%, while saturated fatty acids were 22.72%. Additionally, the major fatty acid present in tomatoes was linoleic acid, taking up to 51.91% of the total fats, followed by oleic acids and palmitic acids, which were 18.5% and 16.32%, respectively.<sup>[76]</sup> It is interesting that the risky ratio of *n*-6: *n*-3 poly unsaturated fatty acids in tomato wastes was 12.56:1, which was relatively moderate compared to various standards.<sup>[77]</sup>



## Glycoalkaloids

Glycoalkaloids, which often refer to the secondary metabolites in the Solanaceae family, can be formed as two compounds, including tomatine and solanine.<sup>[78,79]</sup> The major function of these metabolites is to protect phytopathogens and to exhibit significant function in animals and human beings. As for the tomatine, which mainly consists of the  $\alpha$ -tomatine and dehydro-tomatine, it is mainly stored in nonmature tomatoes (500 mg per kg fresh weight), while the red tomatoes contain a lower content of these compounds (5 mg per kg fresh weight). On the contrary, the ripened red tomatoes have a higher level of Esculeoside A, containing 9–53 mg per 100 g fresh weight.<sup>[80]</sup> Moreover, it also has been suggested that factors such as cultivars and agronomic conditions will affect the content of both glycoalkaloids compounds in tomato fruits.

## Anti-nutritional compounds

Plant-based foods also showed side effects on human health in some cases. As for tomatoes, excessive consumption will also contribute to some undesirable symptoms (Table 3). Several related components resulting from those side effects will be discussed below.

## Organic acid

First of all, the citric and malic acids, which are the main organic acid in tomato products,<sup>[30]</sup> are likely to contribute to the consequences of gastroesophageal reflux diseases (GERD) or heartburn. This condition is caused by consuming a great number of acids, which could be washed back into the gullet, consequently, resulting from symptoms, such as chest pain, sore and burning throat.<sup>[94]</sup> It has been suggested that dietary habits of the high content of tomato consumption showed a higher percentage of GERD levels in patients compared with controls.<sup>[81]</sup> Moreover, the appearance of consuming tomato and the related products in GERD-suffering treatments were reported higher than that in the control group.<sup>[95,96]</sup> Aside from GERD, the organic acids in tomatoes are also related to bladder issues that may enhance the opportunities for uncontrolled urine leakage issues.<sup>[97]</sup> Additionally, excessive consumption of some specific foods, including tomatoes, can cause cystitis, which leads to some undesired bladder symptoms like bladder pressure and burning.<sup>[98]</sup>

**Table 3.** Adverse effects of tomato intake.

Anti-nutritional compounds	Existing portion	Disease and health issues	Ref.
Organic acids: Citric acids and malic acids	Whole fruit	Gastroesophageal reflux disease (heartburn); Urinary problems; Inhibition of the correct absorption of calcium.	[81–83]
Lectins	Tomato seeds	Food allergies; Epithelial lesions.	[84,85]
Pathogenesis-related (PR) proteins: Lyc e 1–4, Lyc e PG, Lyc e chitinase, Lyc e peroxidase, Lyc e glucanase and Lyc ePR23.	Whole fruit	Food allergies;	[86–89]
Dietary oxalate	Tomato juices	Calcium oxalate stone diseases; Urinary oxalate excretion; Decrease the bioavailability of several trace elements	[90,91]
Phytate: K+, Mg2+, and Ca2+	Tomato seeds	Kidney problems; Mineral deficiency	[84]
Glycoalkaloids (tomatine)	Whole fruit	Body aches, arthritis; Inhibition of Acetylcholinesterase; Hemolysis of Red Blood Cells; Antidiuretic Effects.	[92]
Secondary compounds: Saponins	Tomato seeds	Potential atopic dermatitis	[93]
High amount of consumption		Irritable bowel syndrome; Lycopendermia; Migraine	[81]

### ***Protein allergens***

Tomato products are a source of known allergens to specific individuals by consumption and physical contact, causing reactions, for example, sneezing, skin-related issues, red eyebrows/eyelids, itching throat, and swelling of mouth and face.<sup>[99]</sup> However, there have been identified few numbers of protein allergens from tomatoes. Firstly, the most capable protein in tomatoes, which was purified and characterized by<sup>[100]</sup> Westphal, et al., is a glycosylated tomato protein. As a result, this type of compound is able to trigger histamine release from basophils. Another allergen that has the same ability to induce histamine release is profilin.<sup>[101]</sup> In addition, other enzymes found in tomato products, including superoxide dismutase, pectinesterase, polygalacturonase, lipid transfer protein Lyc e 3, and so on, showed various allergy-induction abilities.<sup>[102]</sup>

### ***Glycoalkaloids***

Glycoalkaloids, which commonly appeared in eggplant, potato, green tomatoes, and tobacco, can also be toxic sometimes.<sup>[103]</sup> It has been suggested that a small amount of glycoalkaloids can cause pain and disorder symptoms in the gastrointestinal tract. Additionally,  $\alpha$ -Tomatine embryotoxicity is related to the reduced capability of cholesterol and cell membrane.<sup>[104]</sup> Moreover,<sup>[105]</sup> Salehi, et al. conducted an experiment to compare the chance of arteritis, which contributes to the swollen and painful joints, among individuals that are having tomato-based diets and the control group. They found that the individual intaking tomato regularly has a higher chance to be exposed to this disease. Other undesirable inflammation symptoms in terms of arthritis and painful conditions are highly related to the diets of tomatoes and other nightshade plants.

### ***Excessive potassium consumption***

Tomatoes are a type of plants that contain a high concentration of potassium elements, which may pose a threat to individuals with kidney problems. In fact, individuals have a high level of chances to consume excessive potassium from tomatoes, since this ion is five times greater than sodium.<sup>[11]</sup> Therefore, reduced intake of tomatoes in the daily diet should be complemented for individuals suffering from kidney disorders, as excessive consumption of potassium will exacerbate chronic renal dysfunction and damaged renal potassium excretion, eventually causing a life-threatening disorder called hyperkalemia.<sup>[105]</sup> In this condition, serum potassium levels are greater than the normal limits (5.5 mEq/L).<sup>[106]</sup> Therefore, limiting potassium-rich foods and vegetables is a crucial recommendation for the prevention and control of hyperkalemia.

### ***Oxalate and nitrate***

Oxalate is the other risky compound in tomato-based foods, especially in the sauce. This chemical compound tends to react with the calcium in the circumstances, eventually being influential in both the formation and recurrence of kidney stones.<sup>[107]</sup> Therefore, it is highly recommended that the related tomato diets should be avoided for those groups of people who are vulnerable to kidney issues.<sup>[108,109]</sup> Toxic and antinutritional compounds, such as nitrate<sup>[110]</sup> have also been described in varying quantities in tomatoes. Nitrate is non-toxic but the metabolites may be directly related to health issues like infantile methemoglobinemia, carcinogenesis and possibly even teratogenesis.

## **Effects of processing on tomatoes**

### ***Tomato processing***

#### ***Thermal processing***

For tomato products, conventional thermal processing stages play a role in several effects, including prolonging the shelf-life and food safety. In most cases, methods relied on high temperatures are useful for different purposes, such as inactivating microorganisms and enzymes, modifying sensory profile

and properties, as well as concentration for tomato products. During several steps, there appear to be changes in terms of appearance, nutrition, sensory and composition properties that could affect the quality of final products. For instance,<sup>[111]</sup> Crozier, et al. demonstrated that treatments such as frying, boiling, or microwaving are able to get rid of about 35–78% of the quercetin conjugates from initial materials. As for the interpretation, flavonols were likely to be degraded or extracted and further resolved into boiling water. This tends to be significantly influent tomato by-products, as related products including tomato juices and purees are excellent sources of these compounds. Therefore, it has been observed that thermal processing that contributes to enzymatic hydrolysis could help to hydrolyze quercetin conjugates and dramatically increase the free quercetin content by more than 28%.

A wide range of bioactive chemicals can be found in numerous types of products. Tomato juice and puree, for example, have flavonol concentrations of 15.2 to 16.9 mg/L and 16.6 to 72.2 mg/kg fresh weight, respectively.<sup>[112]</sup> Canned tomatoes, on the other hand, are known to be a poor source of flavonols.<sup>[113]</sup> Furthermore, original manufacture has a significant impact on bioactivity. Flavonol content in fresh fruits collected from various places ranged from 1.3 to 22.2 mg/kg fresh weight.<sup>[112]</sup> The effects of heat treatments on bioactive components in tomato products varied depending on the technology used and the end products.<sup>[114]</sup>

There are some differences in total phenol levels in processed tomatoes. The total phenolic content of tomato homogenate was observed to be steady after being heated to 88°C for 2, 15, and 30 minutes.<sup>[115]</sup> Similarly,<sup>[116]</sup> Jayathunge, et al. claimed that heating tomato juice to 95°C for 20 minutes has no effect on the phenolic chemicals in the final product. Other research, however, found that the phenolic content of heat-processed tomato purees changed. Because the phenolics in the tomato matrix were liberated throughout the procedure, the total phenolic compounds in tomato juice increased after being heated to 80°C for 20 minutes. In the research, however, lower phenolic findings of 43% for red tomatoes and 28% for yellow tomatoes were detected during puree manufacture.

### **Non-thermal processing**

Non-thermal processing including steps like cutting, homogenization, peeling, and so forth, tends to impact the antioxidant components.<sup>[117]</sup> Lana and Tijskens, for example, evaluated the antioxidative capability of fresh-cut tomatoes and hypothesized that fresh-cut tissues are primarily exposed to oxidative stress, resulting in membrane damage and changes in antioxidant component composition and concentration. What is more,<sup>[118]</sup> Capanoglu, et al. found that the “breaker” or homogenization step significantly changed the biochemical composition in industrial processing, as shown by the results of Principal Components Analysis (PCA) of untargeted metabolomics data obtained for tomato paste production steps. Similarly,<sup>[119]</sup> Gahler, et al. studied home-preparation methods including peeling, tomato soup preparation, and so on, as well as three various processes in tomato juice manufacturing, including sifting, homogenization, sterilizing, filling, and pasteurization. The results revealed that homogenizing the tomato products boosted their hydrophilic antioxidant capacity. The actual mechanism, however, is still unknown.

Consumers may prefer to remove specific sections of the tomato fruit, such as the skin, calyx, and seeds while consuming tomatoes directly. Tomato skin, on the other hand, has been shown to have much higher quantities of bioactive compounds than tomato pulp.<sup>[120,121]</sup> It is explainable by<sup>[121]</sup> Toor and Savage that UV radiation tends to damage DNA and cause the formation of UV light-absorbing bioactive compounds, such as flavonoids and phenolics, mostly in the plant’s epidermal tissues. To be specific, the tomato skin contained 98% of fruit flavonols as conjugated forms of quercetin and kaempferol.<sup>[15,122]</sup> Furthermore, there are few studies were focused on tomato seeds, while the importance of investigating the antioxidant level of other fractions of tomato, including calyx, columella, and jelly parenchyma as well as epidermis and pericarp are supposed not to be ignored.<sup>[122]</sup> Mounet et al. studied the other parts of tomatoes and found that carotenoids, flavonoids, and other chemicals were identified in significant concentrations in tissues that are typically

eliminated during tomato processing, such as the calyx and skin. During the preparation of tomatoes into a paste, for example, about one-third of the entire weight of tomatoes is lost in the form of skin and seeds.<sup>[66]</sup>

It has been reported that there appears to be a dramatic loss of phenolic compounds of the whole fruit through disposing of the tomato peel and seeds during processing.<sup>[118]</sup> Specifically, getting rid of the two parts through production resulted in a loss of 4.6% lycopene, 8.6%  $\beta$ -carotene, and 93.3% lutein. The increased loss is most likely due to oxidation processes that occur throughout the manufacturing procedure.<sup>[118]</sup> The increase in rutin and total flavonoid content of the tomato material during the breaking process, when the tomatoes are cut into small pieces and then homogenized, was another finding from this study. The continuance of flavonoid synthesis as a reaction to injury is thought to be the cause of this rise.<sup>[118]</sup> Other fruit types, such as lettuce, apples, and potatoes, were also observed to find the same tendency.<sup>[123]</sup> Freshly sliced tomatoes, on the other hand, showed lesser antioxidant activity than the entire fruit.<sup>[117]</sup> However, at the conclusion of the storage time, they noticed an increase in hydrophilic antioxidant activity, which they speculated was due to some sort of repair or recycling mechanism.

### **Bioavailability of tomato and processing effects**

Bioavailability is a significant concept in terms of functional foods that are increasingly popular in developing new products. It has been shown that several factors tend to affect the bioavailability of antioxidants. In human bodies, there are four main factors proven that will affect antioxidant bioavailability,<sup>[124]</sup> including antioxidant compounds related ones such as chemical properties, structure, linkage, etc.; food-related like matrix and processing; the fruit-related factors like genetics; and also external factors like food availability, environmental effects. Among these, the chemical structure of the aglycone and the kind of glycoside are two of the most significant variables of bioavailability. Varying glycosidic variants of the same aglycone have different bioavailability.<sup>[125]</sup> Some antioxidant groups, such as carotenoids and polyphenols, deserve special attention in the case of tomatoes and they are prevalent in this fruit and can perform a variety of functions that have a major impact on human health. The impact of tomato processing on the bioavailability of different compounds was investigated in this area.

As for the impact of processing on bioavailability in tomato plants, it can be utilized to improve the bioavailability of phenolic chemicals in plant-based diets (Table 4). There are two main requirements for this: (i) reduced processing-induced phenolic compound degradation and (ii) minimal matrix modifications, such as disruption of molecular connections, resulting in increased phenolic compound release and/or absorption in the gastrointestinal system. In most cases, the second condition can be met by a variety of methods, including mechanical processing that causes solubility changes or particle size reduction, an enzymatical or chemical treatment that inhibits food matrix interactions, and processing processes that destroy the matrix. However, many experts believe that using temperature will have a negative impact on phenolic stability in the majority of situations. As a result, food processing that does not involve high temperatures gains a competitive edge. Nonthermal processing is worth mentioning separately because it can be used in place of traditional thermal processing. When developing a plan to improve the bioaccessibility and bioavailability of phenolic compounds, single or combined food processing technologies may be explored, depending on the predicted impact of each technology, as well as the needs of the food product.

However, the conflicting findings obtained using the same technology suggest that the effects of phenolic bioavailability can easily shift from positive to negative depending on the operating conditions, as well as the nature of the phenolic compounds and the matrix of the plant-based food. Under specific operating conditions, the application of PEF or HPP resulted in the increased bioaccessibility of phenolic compounds in plant-based fruit beverages with respect to heat treatment. The results varied depending on the matrix type (water-fruit juice, milk-fruit juice, or soy-milk juice) and the phenolic chemical group (total phenolics, total flavonoids, or total phenolic acids). As a result, food

**Table 4.** The effects of processing on tomato products subjected to both *in vivo* and *in vitro* bioavailability studies.

Bioactive compounds	Study type	Processing	Changes vs. Fresh tomatoes	Ref.
Chlorogenic acid	<i>In-vitro</i>	Tomato paste	Slightly increase	[126]
		Tomato puree	Slightly increase	
		Tomato juice	Slightly increase	
		Drying	Slightly decrease	
		Chopping	Slightly decrease	
		Cooking	Slightly decrease	
		Industrial processing	No difference	[23]
Naringenin	<i>In-vitro</i>	Heat treatment	Lower amounts or absence	[126]
		Home processing	Significantly increase	[23]
		Industrial processing	Significantly increase	
Rutin	<i>In-vitro</i>	Tomato puree and juice	Lower	[126]
		Industrial processing	Slightly increase	[23]
Lycopene	<i>In-vivo</i>	Tomato paste	Slightly increase (2.5 fold)	[127]
		Tomato puree	Increased by 18%	[128]
		Tomato juice	Increased by 23%	[129]
	<i>In-vitro</i>	Tomato powder	Dramatically increase (30 fold)	[130]
		Cooking	Significantly decrease	[131]
		Short thermal treatment (96°C 30 s)	Enhanced by 38%	[132]
β-carotene	<i>In-vivo</i>	Tomato sauce	Increased (60 fold)	[133]
		Boiling (10 min, 100 °C)	Significant increase ( $p < 0.01$ )	[134]
		Microwave-cooking (50 s, 800 W)	Significant increase ( $p < 0.05$ )	
		Grilling (10 min, 800 W)	Significant increase ( $p < 0.01$ )	
	<i>In-vitro</i>	Hot air drying: 60–100 °C	Degradation followed the first-order reaction.	[135]
		Blanched peel	Higher content	[136]
		Blanched flesh	No difference	
Volatile compounds		Thermal processing	Hexanal and (Z)-3-hexenal experienced a significant decrease (>70%) ( $0 < 0.05$ ).	[132]
		High pressure (800 MPa and 60°C)	(E)-2-hexenal significantly increased (20%) ( $0 < 0.05$ ).	[137]
		High-intensity pulsed electric field (HIPEF) processing	The loss almost all volatile compounds. Increased: linalool, 6-methyl-5-hepten-2-one, geranylacetone and 2-isobutylthiazole.	[138]

processing has intriguing potential as a technique for increasing phenolic component bioavailability, but further investigation of the effects under various operating circumstances is required to determine the best strategy for each food product.

## Health benefits of tomato

The generation of reactive oxygen species (ROSs), which refers to both free radicals and non-radicals, is inevitable for the aerobic metabolism of the body. In cells, ROSs can cause lipid and protein oxidation, DNA strand break and base modification, and modulation of gene expression.<sup>[139]</sup> There is a need for aerobic organisms to produce a series of enzymatic or non-enzymatic mechanisms to neutralize those ROSs, using superoxide dismutase, glutathione peroxidase, and catalase.<sup>[140]</sup> Antioxidants generally refer to the lowest ability of the substrates to inhibit the oxidation reaction in the body. They are classified into 2 categories, including synthetic and natural ones.<sup>[18]</sup> It is of great significance to utilize antioxidants to prohibit free radicals from donating electrons, thus preventing all kinds of diseases in both plants and animals.

Regularly consumption of tomatoes provides naturally occurring antioxidants that are essential for disease prevention and inhibition of oxidation. Reactive oxygen species (ROS) are directly relevant to oxidative stress, including neoplasia, atherosclerosis, and neurodegenerative diseases, through oxidative damage of cells and forming disorders.<sup>[141]</sup> As mentioned before, tomato is an excellent source of bioactive compounds, such as polyphenols, carotenoids, and flavonoids. They are associated with inhibitions of the initiation and propagation steps of oxidizing chain reactions, followed by the

**Table 5.** Effects of bioactive compounds occurring in tomato.

Compounds	Main effects	Ref.
Lycopene	Control of oxidative stress and inflammation (production of IL-10 and inhibition of IL-6 and IL-8). Cancer inhibition (prostate, breast, colorectal, endometrial, lung, oral, and pancreatic) Other effects: Cardiovascular Disease; Effect of UV-induced sunburn; Therapeutic effect on asthma.	[143] [13] [143]
β-Carotene	Prevention of photooxidative damage Inhibition of atherosclerosis; Prevention of myocardial infarction Eye health and improvement of symptoms in ARMD	[143] [144]
Rutin	Anti-inflammatory effect: ability to quench free radicals.	[145]
Lutein	Prevention of age-related macular degeneration by increasing of DNA resistance to endogenous damage and repair.	[144]
Vitamin E	Protection against cardiovascular diseases (inhibition of NF-κB signaling). Enhanced humoral and cellular immune responses; reduced risk of Alzheimer's disease. Membrane repair by preventing the formation of oxidised phospholipids. Reduced risks of type 2 diabetes and prostate cancer. Prevention of retinopathy and cataracts. Reduced risk of myocardial infarction.	[145] [11,146]
Vitamin C	Reducing lead toxicity and inducing faster wound repair Facilitating the process of glucose and insulin uptake in diabetic individuals. Decreasing the risk of stroke and heart diseases	[105]
Quercetin	Anti-Inflammation and Promotion of Immunity: mast cell stabilizing and gastrointestinal cytoprotective activity; immunosuppressive effect on dendritic cells function.	[147]
Glycosides of quercetin	Neuroprotective Effects and antagonize oxidative stress Anti-inflammatory effect	[148] [143]

capability of combining with metal ions and inactivation of Fenton reaction.<sup>[142]</sup> Furthermore, a high quantity of vitamins like citric acid and D vitamins in tomatoes are proven to reduce the risk of various cancers and cardiovascular diseases (Table 5).<sup>[149]</sup>

Considering that dietary phenolics have shown numerous health effects in reducing cardiovascular disease, Alzheimer's, or certain types of cancer,<sup>[17]</sup> the interest in both tomato diets and phenolic compounds has been improved. Other than that, tomato wastes produced during processing have also been proved that the bioactive phenolic extracts have antiproliferative activity, further impacting on HeLa (cervix epitheloid carcinoma), MCF7 (breast adenocarcinoma) and MRC-5 (fetal lungs) cell lines.<sup>[14]</sup> When it comes to vitamin C, which is also a source of bioactivity, the antioxidant effects are generally provided by donating electrons to protect lipid membranes and proteins from oxidative damage.<sup>[60]</sup> Additionally, vitamin C is able to improve the synthesis process of collagen by collaborating with 2 essential enzymes in the skin, making this element a health promoter in terms of skin care. The positive effect on ameliorating neurodegenerative diseases was also reported.<sup>[150]</sup>

Next, it has been reported that the carotenoid content in tomatoes is responsible for various chronic diseases. This may be due to carotenoids being able to modulate the immune response and stimulate intercellular signaling pathways.<sup>[151]</sup> What is more, carotenoids also possess pro-vitamin A activity, regulate cell cycle and apoptosis, and could modulate many physiological steps, thus providing resistance to various diseases. Furthermore,<sup>[78]</sup> Pinela, et al. suggested that the lycopene showed significant bioactive capacity and cardiovascular disease therapy effects. Other than that, a higher content of lycopene is also associated with reducing prostate cancer risks.<sup>[152]</sup> Additionally,<sup>[153]</sup> Wu, et al. found that consuming a great amount of lycopene in a daily diet positively affects brain lesions, as the antioxidant and lipophilic traits of these compounds could prevent oxidative stress.

### **Neuroprotective activity**

Several studies revealed the neuroprotective effect of tomatoes. *Lycopersicon esculentum* leaves consist of potential compounds which produce protection from glutamate-induced neurotoxicity. The mechanism relies on regulating the nicotinic receptors and membrane potential of



mitochondria.<sup>[154]</sup> A compound named lycopene found in tomatoes is involved with a variety of health-promoting effects. Neurodegenerative disorders can be ameliorated with the potential treatment of this compound. In addition to that, it serves as a protective measure against toxic substances floating in the air. Toxin provoked neurotoxicity can be reduced drastically with the help of lycopene.<sup>[155]</sup> Lycopene enhances the protection of the nervous system through a cascade of Nrf2/HO-1 signaling pathways.<sup>[156]</sup> In a particular study when lycopene was administered on 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine induced animal model at a dose of 5, 10 and 20 mg/kg, it helped deficiency of striatal dopamine, as well as, down-regulated the oxidative stress and suggested it to be a potential agent for Parkinson's diseases.<sup>[157]</sup> It helped alleviate spinal cord injury.<sup>[158]</sup> A comprehensive study on tomatoes and its isolated compound demonstrated the preventive potential of neurodegenerative diseases.<sup>[159]</sup> Tomato seed extract attenuated the oxidative stress in the central nervous system thereby increasing the cognitive function in mice.<sup>[160]</sup> A study conducted on *Drosophila melanogaster* showed suggested potential inhibition of neurotoxicity and oxidative stress.<sup>[161]</sup> The abundance of carotenoids in the tomato is responsible for most of these effects related to the prevention of neural toxicity.<sup>[162]</sup>

### **Antioxidant activity**

Epidemiological data shows that perceived health benefits are a result of the presence of many antioxidant molecules, including carotenoids, lycopene, ascorbic acid, vitamin E, and flavonoids. Eight components namely, vitamin C, vitamin E, flavonoids, lycopene, carotenoids and phenolic acids, of tomato that contribute to its nutritional quality were investigated in the context of breeding programs aimed at developing nutritionally better genotypes. Twelve advanced tomato breeding lines and six open-pollinated cultivars were produced under rigorous supervision and their antioxidant content was determined. Among the 18 genotypes analyzed, ten had a high level of total carotenoids, six had a high level of  $\beta$ -carotene, nine had a high level of lycopene, and fifteen had a high level of flavonoids, and two had a significant amount of vitamin E.<sup>[163]</sup> In research, the antioxidant capacity of nine distinct tomato varieties was tested using the DPPH and ABTS assays. The presence of ferulic acid, caffeic acid, and lycopene resulted in a substantial antioxidant effect. Similarly, another research conducted with the help of DPPH and the beta-carotene bleaching method revealed the potential antioxidant capacity of tomatoes.<sup>[164]</sup>

### **Anticancer activity**

Tomato showed anti-carcinogenic properties mostly because of lycopene.<sup>[165,166]</sup> Also, high-performance liquid chromatography (HPLC) and Fourier transform infrared (FTIR) revealed the leave extract contains compounds which can exert anticancer activity.<sup>[167]</sup> However, oligosaccharides from tomatoes were found to be associated with the prevention of gastric cancer. Inhibited the AGS cell lines at an  $IC_{50}$  of 3.4  $\mu$ g/mL and 30  $\mu$ g/mL dose causes significant inhibition.<sup>[168]</sup> The cherry tomato efficiently blocked the growth of HepG2 and HeLa cell lines.<sup>[169]</sup> Tomato also restricted the breast cancer cell line, MCF-7, with the  $IC_{50}$  value of 5.85  $\mu$ g/mL (Fig. 2).<sup>[170]</sup> Nanoparticles retrieved from tomato is involved in anticancer potential against cervical and colorectal cell lines.<sup>[171]</sup> Cancer-inducing insulin-like growth factor-1 was reduced significantly through the consumption of dietary tomatoes.<sup>[172]</sup> Tomato is reported to possess a polyphenolic compound named ferulic acid.<sup>[17]</sup> Ferulic acid therapy lowered the viability of breast cancer cell line MDA-MB-231, enhanced apoptosis, and inhibited metastatic potential. Additionally, it was revealed that reversing the epithelial-mesenchymal transition regulates ferulic acid's anticancer efficacy and its function in metastasis suppression. Consistent with the *in vitro* results, the anticancer activity of ferulic acid was also shown in an MDA-MB-231 xenograft mice model, where tumor volume, weight, and apoptosis were considerably lowered.<sup>[173]</sup> The genetic investigation elucidated the anticancer agent's mode of action. Ferulic acid was shown to suppress cell proliferation in PC-3 cells by raising the expression of ATR, ATM,



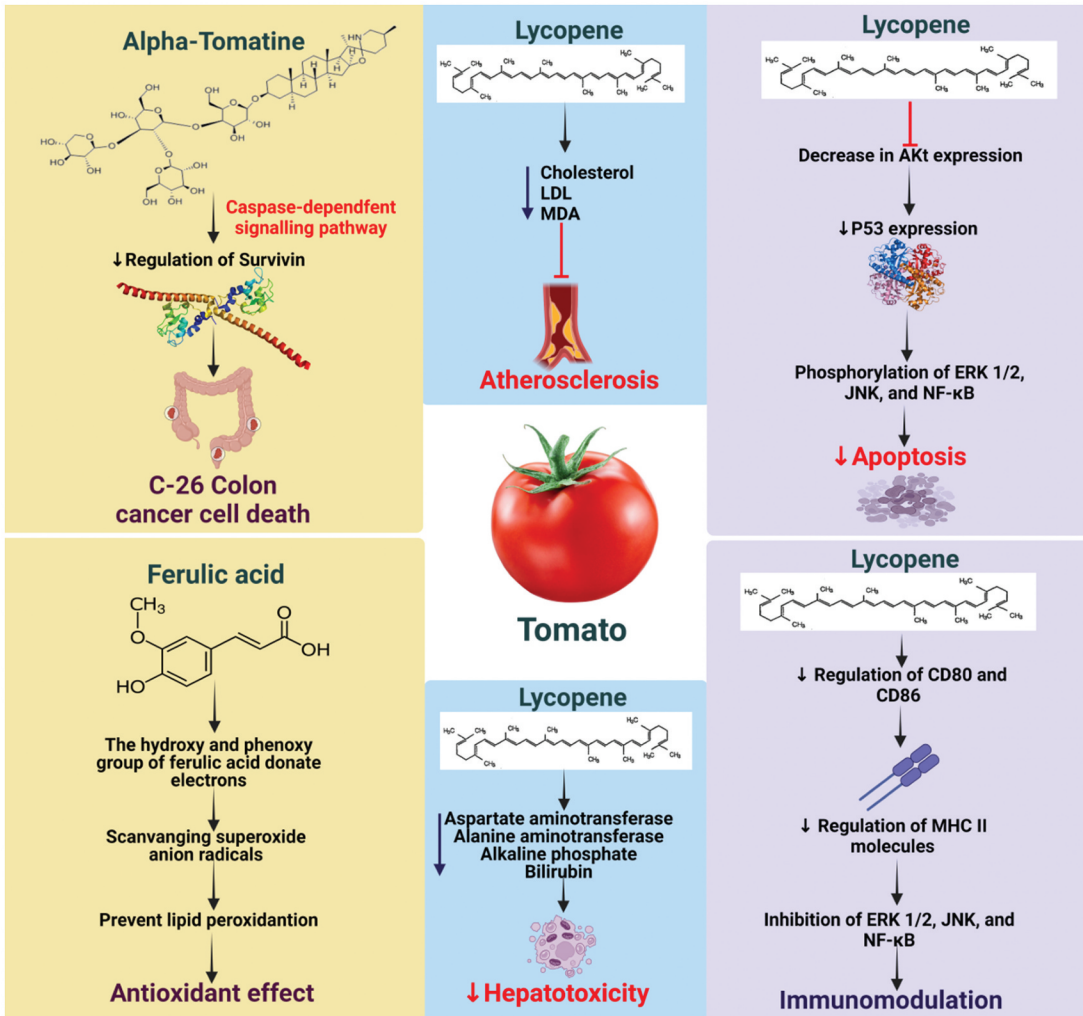


Figure 2. Prospective health benefits of tomato.

CDKN1A, CDKN1B, E2F4, RB1, and TP53 as well as lowering the expression of CCND1, CCND2, CCND3, CDK2, CDK4, and CDK6. Ferulic acid, on the other hand, inhibited cell proliferation in LNCaP cells by raising the expression of CASP1, CASP2, CASP8, CYCS, FAS, FASLG, and TRADD and lowering the expression of BCL2 and XIAP (Fig. 2).<sup>[174]</sup>

### Anti-obesity effect

Vinegar of tomato when administered at a dose of 14 ml/kg to mice model, it drastically attenuates the level of free fatty acid and triglyceride aggregated within the tissue and blood stream thereby down-regulate the visceral obesity.<sup>[175]</sup> Also, tomato consumption before the meal helps individuals regulate blood sugar levels, fat aggregation and cholesterol in a positive way.<sup>[176]</sup> Special vinegar made from tomato treated with 3T3-L1 cells which suggested that it helps deplete adipose tissue and lipid formation and acts as an anti-obesity candidate.<sup>[177]</sup> The weights of epididymal adipose tissue and liver were much lower in mice given a high-fat diet with green tomato extract than in an animal model fed a high-fat diet alone. Serum total cholesterol and low-density lipoprotein cholesterol levels were

significantly lower in mice given green tomato extract, but liver total cholesterol levels were significantly lower in mice fed a high-fat diet with green tomato extract. The phosphorylation of adenosine-monophosphate-activated protein kinase (AMPK) and acetyl-CoA carboxylase was dramatically increased in the livers of mice given a high-fat diet with green tomato extract, but HMG-CoA reductase expression was significantly lowered. Green tomato extract significantly reduced the expression of peroxisome proliferator-activated receptor-gamma, CCAAT/enhancer-binding protein alpha, and perilipin in the adipose tissue of mice given a high-fat diet in combination with green tomato extract (Fig. 2).<sup>[178]</sup> Supplementation with lycopene and tomato powder reduced hepatosteatosis and adipocyte hypertrophy caused by a high-fat diet. Lycopene and tomato powder inhibited the production of proinflammatory cytokine mRNA in the liver and epididymal adipose tissue caused by a high-fat meal. Lycopene and tomato powder had an anti-inflammatory impact by decreasing the phosphorylation of I $\kappa$ B and p65, which resulted in a decrease in inflammatory proteins in adipose tissue.<sup>[179]</sup>

### **Hepatoprotective effect**

Numerous studies were conducted on tomatoes in order to enumerate the hepatoprotective effect. Elevation in the level of alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase through liver damage induced by carbon tetrachloride were reduced with 20 and 40 mL/kg tomato pulp administration.<sup>[180]</sup> The underlying research suggested that lycopene can be responsible for exerting the hepatoprotective effects.<sup>[181]</sup> Lycopene substantially lowered the increase in blood total bile acid and total bilirubin caused by 17 $\alpha$ -ethinylestradiol, as well as the activities of alanine aminotransaminase, aspartate aminotransaminase, alkaline phosphatase, and gamma-glutamyl transaminase. Additionally, lycopene decreased hepatic levels of thiobarbituric acid reactive chemicals and tumor necrosis factor-, as well as the hepatic activity of myeloperoxidase, which were significantly increased by 17 $\alpha$ -ethinylestradiol. Lycopene raised total protein and albumin levels in the liver and decreased glutathione levels. Additionally, lycopene ameliorated the histological alterations in the liver caused by 17 $\alpha$ -ethinylestradiol. Lycopene's protective effects were equivalent to those of silymarin.<sup>[182]</sup> Additionally, lycopene treatment aids in the restoration of impaired liver function after experimentally induced hepatitis.<sup>[183]</sup> Synergistic administration of tomato and onion extract was found to have beneficial effects in case of liver toxicity.<sup>[184]</sup> Toxicity arises from detrimental metal substances, mercury, lead and cadmium, in lives was reduced by prior treatment with tomato.<sup>[185]</sup>

### **Cardioprotective effect**

Tomato showed a potential cardioprotective effect by ameliorating the atherosclerosis state.<sup>[186]</sup> A survey study suggested that daily intake of tomato and lycopene reduces the risk of heart failure.<sup>[187]</sup> In one study, the *n*-hexane extract of tomato was evaluated for its antioxidant activity in rats with experimental myocardial infarction induced by adrenaline administration. Adrenaline significantly increased the heart's malondialdehyde content, a marker of lipid peroxidation, along with a significant increase in serum aspartate aminotransferase and various grades of necrotic changes in the myocardium. Two doses of tomato *n*-hexane extract were given to rats. In adrenaline-treated rats, pretreatment with tomato extract (1 mg/kg, 2 mg/kg) and vitamin E (50 mg/kg) significantly decreased the malondialdehyde concentration in the heart and significantly decreased the serum aspartate aminotransferase level. Pretreatment significantly reduced myocardial necrosis. Thus, it is suggested that tomato *n*-hexane extract has antioxidative properties that may protect the heart from catecholamine-induced myocardial infarction.<sup>[188]</sup> In mice, the preventive effect of tomato extract and lycopene against acute doxorubicin myocardial damage was examined. Doxorubicin toxicity was shown by an increased blood CPK<sub>MB</sub> level and histopathological findings after a single intraperitoneal administration. Tomato extract and lycopene reduced blood CPK<sub>MB</sub> levels and alleviated cardiac cell damage. These findings imply that tomato extract and lycopene both decrease doxorubicin

cardiotoxicity and may be used in conjunction with doxorubicin to prevent organ harm caused by free radicals.<sup>[189]</sup> When compared to controls, the tomato had considerably reduced blood antioxidant enzyme levels and a very high rate of lipid peroxidation in the coronary heart disease (CHD) group. Simultaneously, researchers noticed considerably greater lipid levels in the CHD group than in the controls. Sixty days of tomato supplementation in the CHD group resulted in a substantial increase in blood enzymes involved in antioxidant activity and a reduction in the rate of lipid peroxidation, but no significant change in lipid. These results indicate that tomato lycopene may have significant therapeutic promise as an antioxidant in CHD.<sup>[190]</sup>

## Conclusions

To conclude, the indispensable nutrition value of plant-based foods is predominantly due to the presence of bioactive molecules, for instance, polyphenols, flavonoids, tannins, and other phytochemicals. As a source of antioxidants, those ingredients are also responsible for the health-related effects that would positively impact some chronic diseases, such as cardiovascular disease, and certain types of cancers. However, certain compounds that showed anti-nutritional effects, including organic acids, allergic protein, glycoalkaloids, oxalate and nitrate, would pose a threat to the health conditions. It has been stated that the tomato wastes, which generally exist as the form of pomace, are generated from farm to fork. Rather than disposing of the wastes, this review also summarized the possible solution for tomato waste treatments, including feeding animals, addition in food ingredients, and other uses for energy and fuel. At last, in the processing industry, thermal and non-thermal procedures, such as extraction, concentration, and pasteurization, have a controversially impact on the bioactive compounds in tomato products, which mostly, the content has been improved. By and large, although several side effects and neutral health results were proven after consumption, the majority of evidence still suggests that the benefits of consuming tomato-based products far outweigh the drawbacks.

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