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Antioxidant and Nutraceutical Potential of Tomato for Health and Life Quality: A Review

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Abstract: The significance of diet in connection to human health has raised consumer demand for foods high in nutraceuticals, particularly fruits, and vegetables. The antioxidant phytochemicals vitamins A, C, & E, beta-carotene, carotenes, flavonoids, flavones, total phenolic compounds, etc. are just a few of the many antioxidant phytochemicals that tomatoes are a rich source of DNA, protein, and lipid are all severely harmed by oxidant byproducts of normal metabolism. This damage is a potential contributor to aging as well as degenerative and malignant disorders such as cataracts, immune system decline, cardiovascular disease, and a variety of cancers. Flavonoids, ascorbate, tocopherol, and carotenoids, among others, are antioxidant defenses against these harms. The phenolic chemicals found in tomatoes may also function as antimicrobials, aiding in the management of a wide range of infections. Finally, we want to underline how important it is to establish a connection between the unique breeding of tomato plants and genetic research with the production and overexpression of compounds that are beneficial to human health.
Keywords: Antioxidant activity, Bioavailability, Healthy life, phenolics, therapeutic effect.

1. Introduction

Current recommendations to cope with malignant and chronic disorders recommend increased intake of a nutraceutical-rich diet (Chang et al. 2006) including fruits and vegetables (Nothlings et al. 2008; Santos-Cervantes et al. 2007). The bioactive compounds in fruits and vegetables are responsible for human health by increasing in body's defense system; hence promoting life quality (Pila et al. 2010; Timlin and Pereira 2010). Tomato (Lycopersicon esculentum Mill.) is a potential component of a healthy diet because it not only contains nutritional antioxidants such as vitamins A, C, and E, but also a range of non-nutritional antioxidants, such as beta-carotene, carotenoid, flavonoids, flavones, and total phenolic compound, etc. (Zamora et al. 2005; Javanmardi and Kubota 2006). The antioxidant potential of tomatoes is thought to be closely related to their functional quality (Tyssandier et al. 2004). The beta-carotene, lycopene, found in tomatoes play a defensive role (Oshima et al. 1996), as well as ascorbic acid (Lee and Kader 2000), total phenolic compound, and other vitamins (Abushita et al. 1997,) and minerals play the same role. These carotenoids and ascorbic acid are crucial in preventing reactions caused by reactive oxygen species (Lee and Kader 2000; Leong and Shui 2002). The antioxidant properties of tomatoes prevent and postpone the oxidative reactions that result in degenerative illnesses, both individually and collectively (Block et al. 1992). Numerous investigations have demonstrated the potency of these as oxygen quenchers and oxygen scavengers (Giovanelli et al. 1999). Electron donation and cation production are both part of the mechanism of action. While radicle adduct production is a scavenger

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feature. The cation radicles and their radicle adduct are stable and decompose in a gradual bimolecular manner (Miller et al. 1996). Tomato availability and total antioxidants may be influenced by biotic and abiotic factors. Improving one's knowledge of the availability of functional components is key to understanding the possible mechanisms that affect human health and describing the impact that tomatoes have on healthy living (Zhao and Moghadasian 2008; Lafay and Gil-Izquierdo 2008).
This paper provides a summary of the information on tomato fruit's antioxidant capability. Additionally, the significance and biological functions of the antioxidant component in improving human health are discussed. The review also gives a pinched view of dietary intake and pharmacokinetic properties of the functional components present in tomatoes.

2. Antioxidant Components in Tomato

Tomatoes are a rich source of nutritive antioxidants like vitamins A, C, and E, and non-nutritive antioxidants like beta-carotene, flavonoids, flavones, total phenolic compound, etc. In addition to proximate composition, the fruit also contains other valuable phytochemicals that include carotenoids and polyphenols (Tonucci et al. 1995). For instance, carotenoids contain a red pigment lycopene, phytofluene, and phytoene. Flavonol content is also high in fruit skin conjugated in the forms of quercetin and kaempferol up to 98% (Stewart et al. 2000).
Various research studies emphasize the functional compound in fruits and vegetables for human health. The Organizations working on human health emphasize the importance of antioxidant activity for curing diseases like cardiovascular diseases, diabetes, cancer, and obesity (World Health Report 2002; Stapleton et al. 2008). Most compounds especially antioxidants in tomatoes are responsible for curing disease. The antioxidant property of fruit varies greatly due to the enormous variety of species, stages of ripeness, years of growth, climatic conditions, light, temperature, soil, fertilizer, irrigation, and other cultivation, handling, and storage conditions (Yilmaz 2001).

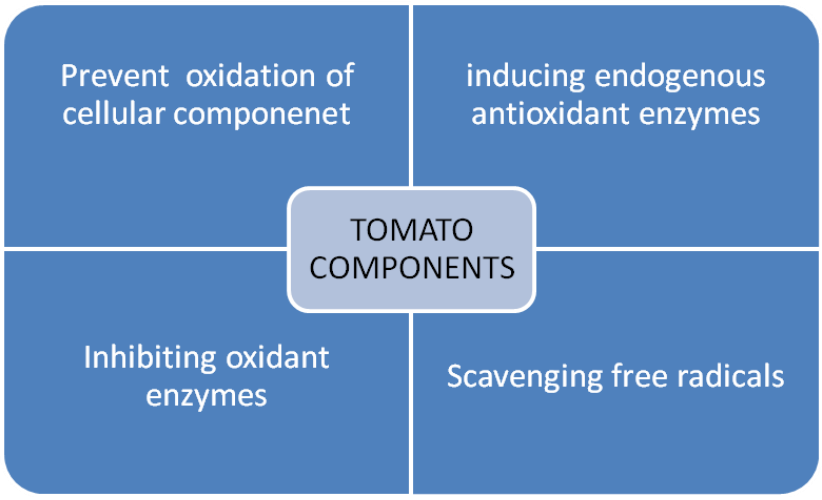

Figure. 1 Property supporting the health-beneficial effect of tomatoes.

Tomatoes and food products that contain tomatoes make it easier for the body to absorb a range of carotenoids, including lycopene and other types of carotenoids (Khachik et al. 2002; Giovannucci et al. 1995; Khachik et al. 1992). These carotenoids are the major source of hydrocarbons that prevent and cure malignant diseases like prostate cancer, breast cancer (Canene-Adams et al. 2005), lung cancer (Feskanich et al. 2000) and other diseases like cataracts, heart diseases (Siemensma 1996; Agarwal and Rao 2000; Rao and Rao 2003), diabetics, hyperglycemia (Boss and Agrawal 2007), inflammation, arthritis (Ames et al. 1993), immune system decline, brain dysfunction (Halliwell 1996; Petr and Erdman 2005) and maintenances of body homeostasis (Kennedy et al. 2006).
Flavonoids are another diverse group of chemicals in tomatoes with an estimated daily intake of 0.023 to 1 gm/day in the human diet. Flavonoids are plant polyphenolic compounds and vary due to the C ring structure predominately including flavanones, flavonols, flavones, and isoflavones, flavanol (Vaya et al. 2003; Aruoma 2003). Most flavonoids are found as glycosides. Glycosides are distinguished by the presence of one or more sugar groups that are glycosidically linked to phenolic groups (Murota and Terao 2003). Clinical trials and

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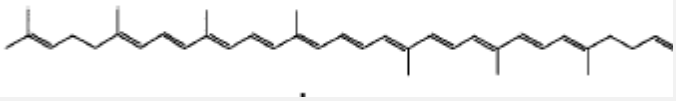
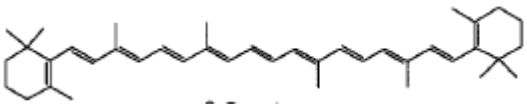
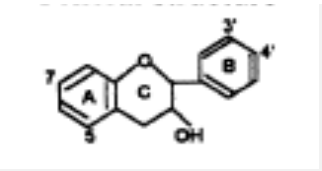
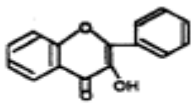
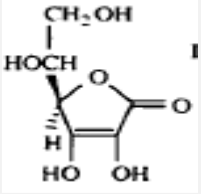
epidemiological studies proved that the consumption of flavonoids plays a potential role in the management and prevention of cardiovascular and cancer diseases (Liang et al. 2001). Numerous members of this family are associated with anti-carcinogenic, anti-inflammatory, cytostatic, apoptotic, antioxidant, anti-aging, and estrogenic activities (Konig et al. 1997; Middleton and Kandaswani 1986; Fotsis et al. 1997; Breinholt and Larsson 1998).

Table 1. Antioxidant component of tomatoes

Component	Structure Formula	Members
Lycopene		
B-Carotene		ζ-carotene, γ-carotene, neurosporene
Flavanol		(+)- catechin (-)-epicatechin Epigallocatechin gallate
Flavonol		Quercetin Kaempferol
L- Ascorbic Acid		

Quercetin is another flavonol containing a sugar group at the 3 positions, commonly distributed in a variety of plant foods (Murota and Terao 2003). Quercetin has been shown in numerous in vitro investigations to have a wide array of biological effects, the most important of which were apoptosis induction, mutagenesis prevention, lipoxygenase inhibition, anti-allergic and superoxide dismutase-like activities, cell cycle modulation, and angiogenesis inhibition (Formica and Regelson 1995).

Tocopherol is also regarded as a functional component, found in tomatoes (Chang et al. 2006). The tocopherols (alpha, beta, gamma, and delta tocopherols) are essential in nutrition because they have vitamin E activity. Although their in-vivo mechanism of action is still poorly known, they have also long been thought of as strong physiological antioxidants (Azzi 2007; Traber and Atkinson 2007).

Table 2. Lycopene, Beta carotene, and Antioxidant content in tomatoes

Tomato varieties	Lycopene	Beta-carotene	Antioxidant Activity (%)	Total Phenolic	Reference
Cherry (Lycopersicum cerasiforme)	122 microgram/100gm	73 microgram/100gm		67 mg/100 g	Guil-Guerrero and Rebolloso-Fuentes 2009; George et al. 2004
Tomato (Lycopersicum esculentum Mill.)	9.25 (mg/100gm)	2.34 (mg/100gm)	38 mg/100ml SEARCH		Khachik et al. 2002; Leong and Shui 2002
Hydroponically greenhouse cluster tomatoes (Lycopersicon Escuesculentl, cv. Clermon)	4.2 mg/100gm		14.92 mmol TEAC/kg.		Javanmardi and Kubota 2006

3. Nutraceutical Component and Biological Effect and Human Health

The nutraceutical activity of bioactive compounds to combat diseases is understood but, the activity against microbes is of greater concern in recent research activities. Increasing interest in personal health made consumers demand safe and healthy food (Paredes-Lopez et al. 2001). Studies in both in vitro and clinical settings have concentrated on the microbiological properties of tomatoes that can prevent Helicobacter pylori chronic infection. Cancer risk is also increased by oxidative load due to chronic infection (Govannucci 1999). Helicobacter pylori are also responsible for elevated DNA oxidation (Baik et al. 1996). It has been demonstrated that extract from the fruit can block the sialic acid-specific attachment of the H. pylori bacteria to the human stomach mucosa. This is an essential phase in the progression of gastric ulcers (Shmuely et al. 2004).

The tomato fruit includes a variety of bioactive substances, including numerous carotenoids and antioxidant vitamins C and E (Khachik et al. 1992). Among common carotenoids, it is believed that the two antioxidants lycopene and beta-carotene are the most powerful at destroying singlet oxygen and free radicals (Woodall et al. 1997; Conn et al. 1993). Oxidative damage may occur because of the imbalance caused by oxidative stress between ROS production and antioxidant defense. The pathology of many degenerative disorders, including diabetes mellitus, cancer, degenerative arthritis, CVD, macular degeneration, Alzheimer's disease, Parkinson's, multiple sclerosis, and Down syndrome, includes the production of excessive ROS, intense antioxidant defense mechanisms, and excessive ROS system activation (Winterbourne 2008; Ames and Gold 1991; Liu and Hotchkiss 1995; Seeram 2008). Human bodies have developed a mechanism to confront stress. The process

comprises exogenous antioxidants from the diet as well as endogenous antioxidants created by the body, such as non-enzymatic and enzymatic antioxidants. Antioxidant and phenolic chemicals show a variety of biologically significant mechanisms to detoxify or scavenge ROS, prevent the generation of ROS, affect the cell cycle, decrease tumor growth, alter signal transmission, control apoptosis, and regulate metabolism (Han et al. 2007; Liu 2004).

If oxidation is found to be an important factor in the development of cancer, the role of nutrition in anti-oxidation will be extremely complicated. In most cases, the effectiveness of various antioxidants is assessed using more complex experimental systems (Bisby and Parker 1995). By reducing α-tocopherol radicals, for instance, the synergistic impact of -tocopherol and ascorbic acid recycle -tocopherol. Such interactions may generate complex synergies that aid antioxidants in scavenging the various reactive oxygen species, hence enhancing the protection they provide overall (Mortensen and Skibsted 1997). Tomatoes may be helpful to human health due to the intricate interactions that take place between the many different carotenoids, ascorbic acid, and polyphenols. These interactions may be the cause of the tomato's positive benefits.

Although it has been suggested that carotenoid compounds, particularly lycopene, may function by preventing reactive oxygen species from harming cellular macromolecules. Additionally, in vitro, research shows that carotenoids inhibit the growth of a variety of cancer cells derived from insulin-like growth factor I. (IGF-I) (Levy et al. 1995). Recent research reveals that there is a favorable correlation between elevated risk of various malignancies and the level of IGF-I in the blood (Chan et al. 1998). A recent study indicated that supplementing tomato products led to a significantly lower endogenous amount of strand breaks in lymphocyte DNA. Other mechanisms are also hypothesized, but most mechanistic findings have come from in vitro investigations (Govannucci 1999; Pool-Zobel et al. 1997).

The ability of bioactive tomato components to decrease and trap free radicals has been studied using in vitro assays; typically, the antioxidant activity of a compound is determined by comparison with a standard reference. Because of the complex interactions that take place among the many distinct carotenoids, ascorbic acid, and other antioxidant polyphenolic compounds found in tomatoes, it is possible that eating tomatoes can be beneficial to human health. These interactions may be what is responsible for the favorable effects that the tomato provides (Huang et al. 2005; Chang et al. 2006).

Type 2 diabetes has been demonstrated to benefit from strawberry fruit. It has been demonstrated that using strawberry fruit in various preparations, including those that are consumed whole, cooled, extracted, and even powdered, can help prevent type 2 diabetes and improve insulin sensitivity, blood vessel inflammation, endothelial dysfunction, and blood sugar regulation. (Putri et al. 2020). Because strawberries have a low glycemic index, diabetics are less likely to experience sudden rises in blood sugar after eating them. Fibers found in strawberries help to regulate blood sugar levels as well (Mortensen et al. 2018).

Table 3. Trolox Equivalent Antioxidant Activities of Polyphenols in Tomatoes

Compound	TEAC (mM)	References
Quercetin	4.7 ± 0.1	Rice-Evans et al. 1996
Kaempferol	1.34 ± 0.08	Rice-Evans et al. 1996
Epicatechin gallate	4.9 ± 0.02	Rice-Evans et al. 1996
Epigallocatechin gallate	4.8 ± 0.06	Rice-Evans et al. 1996
Epigallocatechin	3.8 ± 0.06	Rice-Evans et al. 1996

Attention has been drawn to how nutrition can cause disease because of the prevalence of atherosclerosis and coronary artery disease and the need to slow their progression (Gartside and Glueck 1995; Hu et al. 2000; Joshipura et al. 2001; Kerver et al. 2003). The cardiovascular system is thought to be impacted by several substances found in tomatoes, most notably carotenoid compounds, primarily lycopene (Wilcox et al. 2003; Weisburger 1998). In reaction to ADP, collagen, and thrombin, the powerful antiplatelet components in

tomatoes limit platelet aggregation (Dutta-Roy 2002). Platelets are essential for cardiovascular disease development as well as hemostasis (Libby 2001). The evidence presented suggests that the acute clinical symptoms of coronary atherosclerosis are caused by plaque breakdown and the subsequent development of platelet thrombi (Zaman et al. 2000). Both the stability of atherosclerotic plaques and disease progression may be impacted by platelet activity. We speculate that the tomato's reported cardiovascular advantages may be related to antiplatelet action and, consequently, to the inhibition of platelet function. The primary prevention of cardiovascular disease may benefit from the use of this kind of natural antithrombotic drug (Kennedy et al. 2006).

4. Bioavailability Of Antioxidant Component in Tomato

Figure 2 shows the hypothetical metabolic oxidation of lycopene in people. The research on the chemical oxidation of lycopene with m-chlorobenzene conclusively establishes that this compound undergoes first oxidation at the 1, 2, and 5, 6-positions to produce, respectively, lycopene 1, 2- epoxide and lycopene 5, 6-epoxide. However, lycopene 5, 6-epoxide was extremely unstable, and it underwent cyclization to create a mixture of 2, 6-cyclopropene-1, 5-epoxide A and B. This was the result of the cyclization process. On the other hand, lycopene 5, 6-epoxide was shown to be quite unstable even though lycopene 1, 2-epoxide was found to be quite stable. In human serum, lycopene epoxides and lycopene 5, 6-epoxide have not been identified; nevertheless, 2, 6-cyclopropene 1,5-diols A and B, which are their corresponding cyclic diols, are primarily observed. Lycopene epoxides have also not been found (Khachik et al. 1997; Khachik et al.; 1998). These diols are created by the enzymatic or acidic ring opening of the corresponding epoxides. The oxidation of lycopene in human serum leads to the formation of a new five-membered ring end-group that has three asymmetric centers located at carbon atoms C-2, C-5, and C-6 (Khachik et al. 1998).

There is a possibility that the traces of these chemicals found in tomatoes and products based on tomatoes are responsible for the existence of lycopene metabolites in human serum. Because of the low quantity of these compounds in raw tomatoes and products based on tomatoes Whether or not 2, 6 cyclopropene-1, 5-diols A and B are present in human serum is a mystery that has not been solved (Khachik et al. 1997).

Table 4. Plasma lycopene of tomato products

Product	Lycopene (mg/100gm)	Serving (ml)	Lycopene (mg/100 gm)	Reference
Tomato juice	9.5	250	25	Agarwal and Rao 1998
Tomato ketchup	15.9	15	2.7	Hwang and Bowen 2005
Tomato paste	42.2	30	13.8	Hwang and Bowen 2005
Tomato sauce	14.1	60	8.9	Hwang and Bowen 2005

Lycopene oxidation may result from the natural metabolism of tomatoes, or it may happen as a result of processing tomato-based food products under harsh circumstances, such as extreme heat. These lycopene epoxides can also be produced when lycopene is oxidized in living organisms, a process known as "in vivo" or "in people." In tomatoes with a high acidity level, lycopene 5,6-epoxide has the potential to rearrange into 2,6-cyclolycopene-1,5-epoxides A and B. In the presence of acids in the human stomach, lycopene 5,6-epoxide may undergo a non-enzymatic conversion to produce 2,6-cyclolycopene-1,5-epoxides A and B, which is then followed by hydrolysis to produce each compound's respective diol. This is the outcome of the reaction. The presence of numerous lycopene metabolites in tomatoes and human serum at low concentrations may be due to lycopene's physiological activity as a radical scavenger. One wouldn't anticipate finding the resultant epoxides in the serum if lycopene is truly being oxidized in vivo in humans (Feskanich et al. 2000; Khachik 1997). Consequently, it is more likely that the enzymatic ring opening of the 2,6-cyclolycopene-1,5-epoxides A and B to the observed diols 82 is involved in the metabolic oxidation of lycopene in humans. This type of enzyme may also be responsible for the conversion of lycopene epoxides into 2,6-cyclolycopene-1,5-epoxides A and B, as well as the diols A and B that correspond to these epoxides. This process occurs when lycopene epoxides are rearranged into a different structure. If lycopene 5,6-epoxide is the first product of lycopene

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oxidation in vivo in humans, then the enzymatic conversion of this epoxide to the cyclic diols A and B must be determined first. This conversion can take place with or without the participation of the cyclic epoxides A and B, depending on the circumstances. This transformation can take place either with or without the participation of the cyclic epoxides A and B (Paetau et al. 1998).

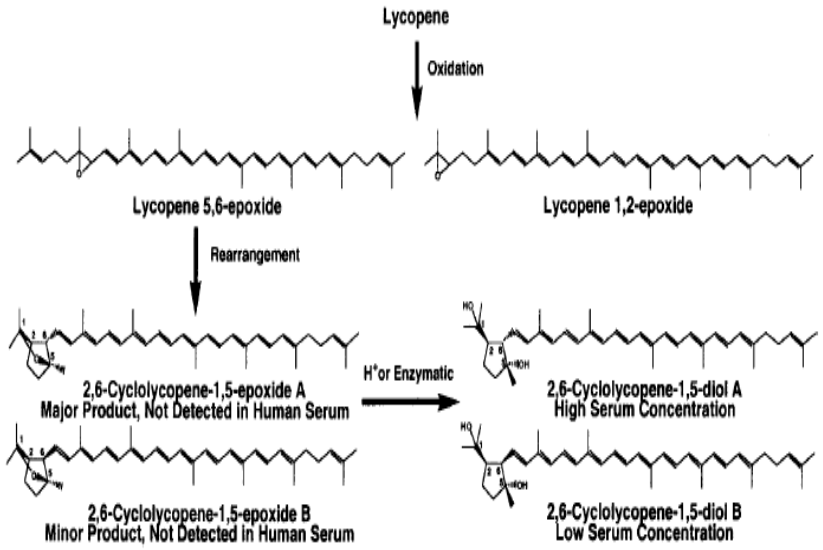

Figure 2. Lycopene metabolism (Khachik et al. 2002)

According to the findings of much epidemiological research, eating tomatoes and products made from tomatoes is connected with a lower risk of developing a variety of cancers (Govannucci 1999). Another study examined the relationship between the consumption of various vegetables regularly and cancer deaths in 1271 senior Massachusetts. According to the study, eating a lot of tomatoes was associated with a 50% decrease in cancer-related deaths across the board. While other vegetables high in carotenoids showed little impact on disease prevention (Rao and Agrawal 2000).

Recent research has analyzed the results of 72 epidemiological studies on tomatoes, tomato-based products, lycopene, and cancer. These investigations included ecological, case-control, dietary, and blood sample-based research (Conn et al. 1993). Numerous research showed a negative correlation between plasma lycopene levels or tomato consumption and cancer. There are strongest associations between different types of cancers, especially prostate, lung, and stomach. On the other hand, there was evidence of connections between cancers of the pancreas, colon and rectum, esophagus, oral mucosa, breast, and cervix. These findings were held when numerous different study designs and a variety of populations were used. None of the examined studies found evidence of higher cancer risk.

In Italy, case-control research found that eating tomatoes was consistently associated with a lower risk of cancers of the digestive system, particularly stomach, colon, and rectal cancers. The research was carried out by the National Institute of Health. In this study, cases are cancers that have been proven in the patient (Franceschi et al. 1994). Similarly, many epidemiological investigations proved an inverse association between lycopene (estimated intakes or serum levels) and breast cancer risk. However, these observations were not confirmed by other investigators (Jarvinen et al. 1997; Zhang et al. 1997). In a different case-control study, researchers observed that the amount of lycopene found in the serum as well as the amount of lycopene taken in the food had an inverse association with the risk of developing cervical intraepithelial neoplasia. This was the conclusion of the researchers (VanEewyck et al. 1991). In yet another cohort trial, researchers showed that the levels of lycopene in serum had an inverse relationship with the chance of developing bladder cancer (Rao and Agarwal 1994). Lycopene status appears to be inversely related to cancer risk, which can be increased by consuming foods high in this carotenoid as well as taking supplements.

Another study conducted in Hawaii found a significantly lower incidence of lung cancer; nevertheless, the same study combining case and control groups found only a little negative correlation between lycopene

consumption and the risk of developing lung cancer that did not meet the statistical criteria for significance (Le Marchand et al. 1989; Le Marchand 1993). Only 29% of the lycopene intake in this population was reported to come from tomatoes. The inconsistent findings regarding tomato consumption and lycopene levels suggest that either lycopene derived from foods other than tomatoes is difficult to get or the health benefits of tomato consumption are attributed to compounds other than lycopene.

One study that discussed mesothelioma (peritoneal or pleural cancer) was available (Muscat and Huncharek 1996). People who consume tomatoes or tomato juice 16 times or more per month have a risk that is reduced by forty percent when compared to people who do not consume either food item. Only 1.7 percent of the control participants and 9% of the case subjects said they didn't consume tomatoes or tomato juice, indicating that tomato product non-consumers have a relatively significant chance of developing mesothelioma.

The case study from China and Italy reported (Franceschi et al. 1994; Hu et al. 1991; Franceschi et al. 1997) about a 60% reduction in the risk of both colon and rectal cancers associated with higher tomato consumption. Lycopene and lutein, but not b-carotene, in a mouse model of N-methyl nitrosourea-induced colonic aberrant crypt foci, medication exhiexhibitedicacy against this premalignant lesion in dosages that were regarded to be quite low. This activity was shown in a mouse model (Narisawa et al. 1996).

Few studies on tomatoes and lycopene with esophageal cancer have been conducted (Table 5). In Iran, where men are more likely than women to suffer esophageal cancer, according to one study, males who consume tomatoes regularly had a much lower risk of developing prostate cancer by 39%. Nevertheless, the researchers found no association between the consumption of tomatoes and the risk of developing prostate cancer in women (CookCook-Muzaffaral. 1979). In the United States, the on a ly study that is diet-study (Brown et al. 1998) regarding this cancer, researchers discovered a 30% reduction in the risk of esophageal cancer associated with heavy consumption of tomatoes in men. However, this reduction was not statistically significant. A serum bank study found that case patients with oral, laryngeal, or esophageal cancer had a 5% lower mean pre-diagnostic serum lycopene level than control subjects; however, based on only 28 case-patients with esophageal cancer, case patients had a 16.4% lower lycopene level. This finding was not statistically significant (Giovannucci et al. 1995).

The findings of the US Health Profession Follow-up Study revealed that lycopene from various tomato products was inversely related to the risk of prostate cancer. It has been found that eating at least 10 servings of tomato products each week lowers the risk of cancer by 35%, with the preventive effects being much more pronounced for more severe or aggressive prostate cancer (Giovannucci et al. 1995). Additionally, recent case-control and cohort studies, including research on carotenoids, particularly beta-carotene, found an inverse relationship between serum and tissue levels of lycopene and the risk of developing prostate cancer (Nomura et al. 1997; Gann et al. 1998). There were four different cohort studies, and each of them came to its conclusions about the association between eating tomatoes or lycopene and an increased chance of developing prostate cancer. Consumption of tomatoes and beans, lentils, and peas was the only thing that was statistically significantly associated with a decreased risk of prostate cancer in a population of 14,000 Seventh-day Adventist men. Tomatoes have also been linked to a lower risk of bladder cancer. There was no link found between eating foods high in beta-carotene and risk (Giovannucci et al. 1995; Mills et al. 1989; Cerhan et al. 1998). In a more comprehensive investigation, researchers found no correlation between the consumption of the carotenoids b-carotene, a-carotene, lutein, and b-cryptoxanthin with an increased risk of prostate cancer. a more in-depth investigation of the diet, but there was a correlation between a high intake of lycopene and a risk decrease that was statistically significant by 21%. The ingestion of tomatoes and products derived from tomatoes, which accounted for 82% of the lycopene, was associated with a 35% and 53% reduction, respectively, in the risk of developing aggressive prostate cancer (Giovannucci et al. 1995). The highest inverse link between prostate cancer risk and tomato sauce was found, however tomatoes and pizza were shown to have weaker inverse associations, but there was no evidence of such a relationship with tomato juice. Initial findings from two separate studies using cohorts (Giovannucci et al. 1995; Mills et al. 1989; Cerhan et al. 1998) also support this finding.

Three studies looked at lycopene levels in serum in connection to cervical cancer (Potischman et al. 1991; Batieha et al. 1993), or precursor lesions (VanEnewyk et al. 1991), while two studies looked at tomato consumption and the risk of cervix cancer (Marshal et al. 1983; de Vet et al. 1991). In one case-control investigation (Marshal et al. 1983), there were three studies conducted that investigated the relationship between lycopene levels in serum and cervical cancer. According to a study by NethNetherlands Vet et al. 1991), women who consumed tomatoes at least thrice per week had a 40% lower risk of developing cervical dysplasia compared to women who did not consume tomatoes.

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There was only one study that published any information on tomatoes or lycopene concerning ovarian cancer, so this is all we have to go on. 35 case subjects participated in this prospective serum-based investigation (Helzlsouer et al. 1996). Even though the case participants' mean serum lycopene levels were 7.4 lower than those of the control, this tiny investigation found no correlation. Before more definitive judgments can be drawn about this cancer, more research is necessary.

Table 5. Pharmacokinetic parameters in human

Type of Cancer	Type of Study	No. of case study	Exposure	%age reduction in risk	Reference
Lungs and Pleura	Case-control	230♂ 102♀	Quintile 5 vs. 1 Lycopene consumption from tomatoes Quintile 5 vs. Quintile 1	29%	Le Marchand et al. 1993
Lungs and Pleura	Case-control (mesothelioma)	94	Tomato/tomato juice consumption, ù16 vs. 0/mo	40%	Muscat and Huncharek 1996
Colorectal	Case-control (colon, rectal)	111 C 225 R	1966 diet (>15 kg/y) 1985 diet (>15 kg/y) ♂ rectal 1966 >20 kg/y	60%	Hu et al. 1993
Colorectal	Case-control (colon, rectal)	955 C 629 R	Quartile 4 vs. 1 Tomato	60%	Franceschi et al. 1997

Esophageal and laryngeal	Case-control (esophagus)	217 ♂ 127 ♀	Raw tomato intake, ≥1/wk vs. <1/mo	39%	Cook-Mozaffari et al. 1979
Esophageal and laryngeal	Case-control (esophagus)	207 ♂	Tomatoes, high vs. low intake	30%	Giovannucci et al. 1995
Prostate	Cohort	773	>10 servings of tomato-based goods per week compared. 1.5 servings per week Tomato sauce consumption, 2-4 vs. 0/wk	21%	Giovannucci et al. 1995
Prostate	Cohort	328	Intake of lycopene in the diet, 718 mg vs. 402 mg 5 raw tomatoes per week vs. 3 per month Cooked tomato consumption, 2/wk vs. 1/mo	35%	Kays 1997
Cervical cancer	Case-control (Cervical dysplasia)	257	Tomato intake, ≥3 vs. 0/wk	40%	de Vet et al. 1991
Ovarian	Cohort	35	Serum lycopene level, >35.2 mg/dL vs. <21.9 mg/dL	7.4%	Helzlsouer et al. 1996

Ingestion of tomato juice prevented male Fischer 344 rats from developing urinary bladder transitional cell carcinomas that were generated by N-butyl-N-(4-hydroxy butyl) nitrosamine (Okajima et al. 1998). Recent research has shown that ingesting lycopene at a concentration of 10 parts per million (ppm) significantly reduces the oxidation of lipids and proteins and appears to protect against colonic preneoplastic lesions brought on by azoxymethane. In the rat colon model, it was also shown that dietary lycopene in the form of vegetable juice was protective against AOM-induced aberrant crypt foci (Arimochi et al. 1999).

Male mouse lung adenomas and carcinomas caused by diethylnitrosamine, methyl nitrosourea, and dimethylhydrazine were considerably reduced by dietary lycopene dissolved in water at a level of 50 ppm (Kim et al. 1997). However, female mice did not exhibit the lung cancer prevention benefits of lycopene. In the same study, dietary lycopene had no impact on kidney or colon cancers. The tobacco-smoke carcinogens benzo[a]pyrene and 4-[methyl]nitrosamino] were not affected by dietary lycopene therapy in another investigation. 1. [3-pyridyl] lung tumor multiplication brought on by 1-butanone in A/J mice (Hecht et al. 1999). The absence of DNA oxidation in this animal was presumably the cause of the lack of protection against benzopyrene-induced lung cancers.

In the study, 12-week-old Wistar rats treated with intraperitoneal ferric nitrilotriacetate (Fe-NTA) (10 mg Fe/kg) had their plasma and prostate carotenoid concentrations on oxidative DNA damage assessed. Plasma concentrations of beta-carotene and lycopene were measured as a function of time in rats that had been given carotenoids intraperitoneally (10 mg kg-1 day-1 of either lycopene or beta-carotene). After receiving an intravenous injection of lycopene or beta-carotene, the peak total plasma concentration was reached three or six hours later, depending on which compound was administered. After five days of treatment with carotenoid therapy, the levels of lycopene and beta-carotene in the prostate were in the range of 0.10-0.51 nmol/g of wet tissue. The amount of 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodGuo) in rat prostate DNA was considerably higher 3 hours after Fe-NTA injection (6.3 0.6 residues/106 dGuo) compared to control rats (1.7 0.3 residues/106 dGuo) using a sensitive method to detect 8-oxodGuo by HPLC/EC. Before receiving Fe-NTA treatment, rats given lycopene or ß-carotene showed a 70% drop in 8-oxodGuo levels, bringing them close to control levels. The buildup of malondialdehyde in the prostate of Fe-NTA-treated rats was 78% higher than that of control rats. Pre-treatment with lycopene or ßcarotene virtually eliminated lipid degradation (Rao and Agarwal 2000).

Atherosclerosis, the condition that underlies heart attacks and ischemic strokes, is thought to be caused in part by the oxidation of LDL, which transports cholesterol into the bloodstream (Witztum 1994; Parthasarathy et al. 1992). Because they can prevent harmful oxidative processes, antioxidant foods are thought to reduce the development of atherosclerosis (Parthasarathy et al. 1992; Hodis et al. 1995). Various epidemiological studies have demonstrated vitamin E's beneficial effects, which are attributed to its antioxidant characteristics (Moriss et al. 1994; Timm et al. 1993). However, multiple studies on dietary interventions using a-tocopherol or b-carotene have shown conflicting findings. Lycopene-related studies have not been carried out.

In several epidemiological studies, a decreased risk of getting CVD has been associated with increased plasma lycopene levels (Petr and Erdman 2005). For instance, In the Kuopio Ischemic Heart Disease Risk Factor Study, researchers investigated the relationship between serum antioxidant levels and the intima-mediated thickness of the common carotid artery (CCA-IMT). The CCA-IMT is a measurement that is associated with the probability of having an acute coronary episode. They found that those who had a cardiac event had lower levels of plasma lycopene than those persons who did not have a cardiac incident (Rissanen et al. 2002; Rissanen et al. 2003). Additionally, a lower mean and maximal CCA-IMT with low lycopene was inversely linked with a greater serum lycopene concentration, leading to an 18% rise in CCA-IMT.

Since 1984, cardiovascular diseases have been the cause of death for one person every minute, resulting in the deaths of half a million women annually and more women than males.27 The Women's Health Study is a trial that is currently being conducted and is randomized, double-blind, placebo-controlled, and two-factorial. The purpose of the study is to investigate how aspirin and vitamin E increase the likelihood of cancer and cardiovascular disease developing in women. Women who consumed 1.5 to 4 servings a week, 4 to 7 servings per week, 7 to 10 servings a week, or 10 servings a week were compared to ladies who consumed the fewest tomatoes overall in the first quintile. The participants were provided with FFQs to fill out. The relative risks of cardiovascular disease (CVD) associated with eating tomatoes were 1.02, 1.04, 0.68, and 0.71 respectively. In addition to this, it was shown that consuming a greater quantity of tomatoes, as opposed to lycopene, was more significantly associated with a reduced risk of developing cardiovascular disease (Sesso et al. 2003).

Antiplatelet aggregation is also linked to tomato consumption. Components of tomato extract seem to inhibit glycoprotein IIb/IIIa and platelet secretory processes, which in turn appears to be connected to the suppression of ADP-, collagen-, thrombin-, and arachidonate-mediated platelet aggregation. After supplementing for 3 hours with a dose of tomato extract equal to 6 tomatoes, they discovered a significant reduction of baseline platelet function, decreasing it from 2.9 1.4% to 20.0 4.9% (Kennedy et al 2006).

Table 6. Pharmacokinetic Parameters in Human Cardiovascular Diseases

Type of Study	Target specie	Dose	Response (Relative risk)	Reference
Double-blind, placebo-controlled 2 _ 2 factorial	Women	1.5 to <4, 4 to <7, 7 to <10, or≥10 a week	1.02, 1.04, 0.68, and 0.71	CaCaninedams et al. 2005
In vitro platelet aggregation	Male and Female. 16 to 60 years of age	18 gm extract syrup	2.9 ± 1.4% to 20.0±4.9% inhibition baseline platelet function	Kennedy et al. 2006

To increase the variety of exposure within the trial, participants in the recent multicenter case-control study (EURAMIC) were drawn from ten different European nations. Only lycopene levels, not b-carotene levels, were found to be protective when several dietary factors were taken into account (Kohlmeir et al. 1997). Lycopene's preventive potential was greatest in those with the highest polyunsaturated fat reserves, lending credence to the antioxidant notion. In a concurrent cross-sectional investigation, it was discovered that decreased blood lycopene levels were likewise linked to an increased risk of mortality from CVD (Kristenson et al. 1997). The epidemiological studies conducted to date have a variety of limitations, including, but not limited to, the heterogeneous population, blood carotenoid levels, duration of the investigation, and illness biomarkers. More research should be undertaken with these study criteria in mind to provide a more definite function for lycopene in disease prevention.

5. Toxicity

A few interventions trials show, in contrast to much observational research, that dietary supplementation with high quantities of carotenoids, including lycopene, has no utility in preventing human disease and may even increase disease incidence for risk groups.

An eating problem called lycopenaemia is brought on by consuming too many tomatoes, which are high in lycopene (Reich et al. 1960). The pigment is secreted by the sudoral and sebaceous glands after consumption and is partially reabsorbed by the keratin layer of the skin (Bonnetblanc et al. 1987). On the forehead, nasolabial folds, palms, and soles, a "yellow-orange" pigmentation was seen. The patient has been experiencing stomach aches for a few months. In actuality, the pigment tends to accumulate in specific regions of the liver and congeals into "fatty cysts," causing microscopic and macroscopic changes to the parenchyma.

Lycopene has been used in rat feeding trials lasting four and fourteen weeks as well as embryotoxicity/teratogenicity research that has all been published as standard repeated dosage animal toxicity data (Jonker et al. 2003). The lycopene beadle formulation was well tolerated by rats in the 4-week study at a dose of 1000 mg/kg body weight/day. At doses of up to 500 mg lycopene/kg body weight/day, rats were treated with a beadle formulation for 14 weeks with no adverse effects. A dose-related orange-red staining of the liver and adipose tissue was seen, particularly in females, and it only partially dissipated after a five-week recovery period. This was detected in both the liver and the adipose tissue. At the high and mid-doses (150 mg/kg body weight/day), there were small alterations in hematological parameters, and, in one sex only, there were changes in the thyroid and brain's relative weights. In this investigation, no morphological or histological changes caused by the therapy were noted. At a dose of 1000mg lycopene/kg body weight/day, the pups' embryotoxicity study found an increase in the number of complete extra thoracic ribs (14th rib). In a recent 13-week oral toxicity trial that complied with GLP standards, rats were given two more synthetic lycopene products by daily oral gavage in water. The products contained a stabilizing formulation matrix that contained

around 10% synthetic lycopene (Mellert et al. 2003). The maximum dose level assessed in the above investigation, approximately 300 mg of lycopene per kilogram of body weight per day, was a NOAEL.
Intake of flavonoids, particularly quercetin, and cancer, particularly lung cancer, were found to be negatively correlated in the Kroon and Williamson (2005) study, which involved approximately 10,000 participants. It appears that bio-phenols are hazardous to cancer cells that are growing quickly but not to healthy cells. Actually, despite the results of a sizeable majority of studies indicating that bio-phenols have no effect, no dietary intervention studies have yet demonstrated a negative effect that bio-phenols have. According to the findings of a toxicological study, the administration of a mega dose of grape seed proanthocyanidin extract equaling 2 grams per kilogram of body weight did not result in any discernible toxicity (Knekt et al. 1997).

6. Conclusion

There has been a growth in research expertise, understanding, and application of practical methodology pertinent to bioactive substances in recent years. This expansion can be ascribed to a variety of sources. The discovery of alternative medicines that utilize tomato compounds for the prevention and management of illnesses caused by antibiotic-resistant bacteria will also be a major future concern in establishing research priorities in the coming years. Tomato compounds with antioxidant characteristics have many potential applications in the food industry and medicine as natural antibacterial agents. In our opinion, the synthesis of chemicals for the sake of nutrition and health should be given a higher priority and more attention. Techniques like plant breeding and genetic analysis come into play here.

7. References

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