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UTILIZATION OF TOMATOES (SOLANUM LYCOPERSICUM L.) TO REDUCE THE RISK OF PROSTATE CANCER: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Prostate cancer is cancer that develops in the prostate gland of the male reproductive system. It is caused by prostate cells that begin to mutate and multiply out of control. Prostate cancer is the most common cancer in men globally after lung cancer. Lycopene has been identified as an antioxidant substance that is potentially an anticancer substance. Lycopersicum is a carotenoid most commonly found in tomatoes (Solanum lycopersicum L.). However, some studies' results for the relationship between lycopene in tomatoes (Solanum lycopersicum L.) with the risk of prostate cancer still show inconsistencies. **Purpose**: This study aims to find out and update the data related to the correlation between lycopene content in tomatoes and the risk of prostate cancer. **Methods**: This research method uses a systematic review method by searching research journals from PubMed, Google Scholar, and Science Direct database with inclusion criteria for analysis. **Results**: As a result, 6 out of 5 similar research journals for analyses related to the correlation between lycopene in tomatoes (Solanum lycopersicum L.) with a reduced risk of prostate cancer. **Discussion**: Prostate cancer patients have a low antioxidant content in their blood, thus increasing the stress of oxidation and lipid peroxidation. Reducing the risk of oxidation requires an intake of antioxidant substances that function as an anticancer substances, one of which is lycopene in tomatoes (Solanum lycopersicum L.). Lycopene serves as a free radical carcinogenesis substance and increases overall antioxidants, thereby reducing oxidative damage to lipids, proteins, and DNA. Although there are still inconsistencies in some studies related to the co-relationship of the two, this study concludes that there is a tendency to a correlation between lycopene in tomatoes (Solanum lycopersicum L.) with drop risk of prostate cancer. **Conclusion:** Thus, effective levels of lycopene in tomatoes (Solanum lycopersicum L.), which should be consumed at a certain time to lower the risk of prostate cancer are still unclear in number and more research is still needed related to this.

Keywords: tomato, lycopene, and prostate cancer.

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INTRODUCTION

Prostate cancer is the most common cancer in men (after lung cancer) and ranks as the fifth largest cause of death globally. Approximately 1,276,106 new cases occurred and caused 358,989 (3.8% of all cancer-induced deaths) in 2018 (Rawla, 2019). Cases of prostate cancer usually occur due to increased age. According to Crawford, eighty percent of prostate cancer patients are over 65 years old. The incidence of prostate cancer in Asia averages about 7.2 per 100,000 men per year. Meanwhile, in Indonesia, the accumulation of prostate cancer patients in central education hospitals located in Jakarta, Surabaya, and Bandung over the last 8 years is 1,102 patients with an average age of about 67.18 years (Decree of the Minister of Health of the Republic of Indonesia, 2018).

According to the American Cancer Society, prostate cancer occurs when the cells in the prostate gland grow out of control. Prostate cancer may have no symptoms at an early stage or have only mild symptoms. The complaints that often occur in patients are difficulty with urination, increased capacity of urine, and nocturia, which is the medical term for excessive urination at night. Other symptoms in the advanced stages of prostate cancer are urinary retention and back pain (Rawla, 2019). Patients can be diagnosed

with prostate cancer during routine rectal examinations (Mazhar and Waxman, 2002).

Identifiable risk factors for prostate cancer include age and race/ethnicity. Other risk factors are external exposure such as ionic radiation, radiation from ultraviolet rays, smoking, food intake, weight, physical activity, and hormones also affect prostate cancer risk (Gann et al., 1999).

One of the causes of prostate cancer is the accumulation of DNA damage caused by some mechanisms, one of the causes is stress oxidative. Oxidative stress is caused by an imbalance between antioxidants and free radical levels. Increased levels of free radicals occur in old age, chronic inflammation, and low levels of antioxidants in the body. The role of antioxidants in preventing various diseases has been a concern in recent years. Antioxidants are said to have a broad scope as anticancer and atherogenic substances. One of the antioxidants that are important to fight oxidation is lycopene, a substance in tomatoes as an essential food source. Lycopene is a tomato carotenoid, an acyclic isomer of β-carotene, which is a hydrocarbon containing 11 conjugated bonds and 2 unconjugated bonds. Lycopene is a very powerful antioxidant and is believed to be an anticancer substance (Agarwal and Rao, 2000).

Fresh tomato fruit has a lycopene content of 30 - 200 mg/kg (Roh et al., 2013) and contains solanine of 0.007 %, saponins, folic acid, malic acid, citric acid, bioflavonoids (including lycopene, α and ß-carotene), proteins, fats, vitamins, minerals, and histamine (Adams et al., 2004).

Some studies have found that the consumption of tomatoes or processed tomato products may lower the risk of some types of cancer. Still, some studies show no significant effect between the consumption of lycopene in tomatoes and the risk of prostate cancer. Nevertheless, there remains a tendency that the intake of lycopene in tomatoes can lead to a reduced risk of prostate cancer (Chen et al., 2015). In a meta-analysis published in 2003 by Etminan et al., there was an inversely comparable effect between lycopene consumption in tomatoes and prostate cancer, but in a study published in 2013 by Chen et al. found no effect between the two (Chen et al., 2015). In 2014 a high-quality, 24-year study with an advanced nested case control (NCC) study was conducted involving 51,529 healthy men in the United States. The study showed that there was a 0.91, 95% lower risk of prostate cancer in those with a high lycopene intake compared with those with a low lycopene intake (HR) of 0.91, a 95% secret interval [CI] of 0.84 to 1.00). The inconsistencies of the above two studies may be related to the difference in their intake levels (Agarwal and Rao, 2000). This systematic review aims to find out and update on the correlation between lycopene content in tomatoes and the risk of prostate cancer.

METHOD

The design used in this study is a systematic review. The articles in this study were obtained from an electronic database published in Google Scholar, PubMed, and Science Direct, published from 2011 to 2021. The keyword structure used in literature study searches is tomato and lycopene and "prostate cancer" and (effect or benefit) not animal. The criteria in this study are articles published in the last 10 years, in English, available in full text, type of research articles, and contain discussions about the influence of lycopene content in tomatoes to reduce the risk of prostate cancer. The steps in this study are summarized in Figure 1.

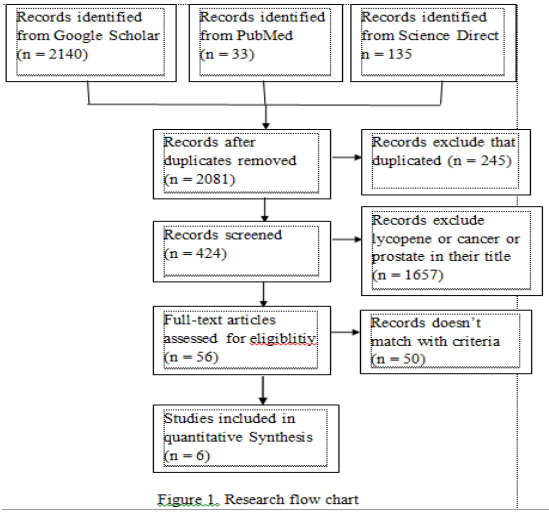

Figure 1. Research flow chart

The number of articles obtained from the Google Scholar database is 2140, PubMed as many as 33, and Science Direct as many as 135 articles. Articles published more than once and published by Google Scholar, PubMed, and Science Direct are marked. After viewing the inclusion criteria, only 2081 articles meet the criteria. Screening is done by looking at the titles that cover the words

"lycopene", "cancer", and "prostate" with the time of publication of the last ten years obtained 424 articles. Filtering is continued by examining the abstract of each article to see the relevance of the article to the topic discussed in this systematic review, then we examine the fully available article. There are 6 articles that meet the inclusion criteria that will be used in this systematic review.

RESULT

Based on articles that meet the criteria for inclusion, lycopene in tomatoes does not have a great effect on the prevention and cure of prostate cancer. The effectiveness of lycopene against prostate cancer is still questionable due to conflicting results from several studies. According to Van Breemen et al. (2011) and Grainger et al. (2015), lycopene consumption may increase plasma concentration and prostate lycopene in men significantly. However, Grainger et al. research stated that food, biological, and genetic factors that affect the concentration of lycopene in the blood and tissues are not yet known, so this study requires more research on the relationship between lycopene and prostate cancer risk.

According to Soares et al. (2019), lycopene is proven to inhibit cell survival, withstand cell cycles and increase apoptosis in prostate cancer cells. Foods with tomato ingredients exhibit strong anti-carcinogenic effects on PC-3 and DU-145 cells which are prostate cancer cells. In vitro experiments conducted by Holzapfel et al. (2013) showed the presence of the chemopreventive effect of lycopene on prostate cancer cells. Lycopene in tomatoes plays a role in decreasing the proliferation and growth of prostate cancer cells. The ability of lycopene to reduce proliferation by increasing cholesterol expenditure in the cell lines tested, where an increase in cholesterol metabolism has been known to be involved in the development of cancer. This discovery is also an indication of the potential for lycopene as an antitumor.

Contrary to the results discussed above, Kristal et al. (2011) showed no influence of lycopene contained in tomatoes on prostate cancer cells. A similar report by Wang et al. (2016) which stated that the intake of lycopene or tomato products was not associated with PCSM (Prostate Cancer SpecificMortality)during long-term follow-up. Research conducted by Holzapfel et al. (2013) through in vivo experiments showed inconsistent results. The diversity of lycopene formulations used in the research and the differences in the object of research can be factors that cause inconsistent results. Therefore, more research is still needed to clarify the effect of lycopene in tomatoes on prostate cancer.

DISCUSSION

Prostate cancer is cancer that develops in the prostate gland of the male reproductive system. This happens when prostate cells mutate and begin to multiply out of control, they can spread from prostate cells to other parts/tissues in the body, such as bones or lymfonodus (Novaldy and Iyos, 2016). Prostate cancer is the second most common cancer in men (after lung cancer) worldwide, accounting for 1,276,106 new cases and causing 3,58,989 deaths (3.8% of all cancer deaths in men) in 2018. The incidence and mortality rate of prostate cancer worldwide is closely related to increasing age by an average of 66 years (Rawla, 2019).

The incidence of prostate cancer in Asia averages about 7.2 per 100,000 men per year. Meanwhile, prostate cancer patients in Indonesia who accumulated in central education hospitals in Jakarta, Surabaya, and Bandung during the last 8 years recorded as many as 1,102 patients with an average age of about 67.18 years. At the time prostate cancer patients came to treatment, 59.3% of them came at an advanced stage. The number of sufferers in 2001-2006 counted twice as much as when in 1995-2000 in RSUPM Dr. Cipto Mangunkusumo and Rumah Dharmais Cancer Disease, with an average number of 70-80 new cases. During the period 2004-2010 found prostate cancer patients as many as 318,193 cases in RSUP Dr. Hasan Sadikin, Bandung. Meanwhile, At Dr. Moewardi Surakarta Hospital, the period 2000-2006 accumulated as many as 30 cases of prostate cancer, with 23 cases still localized, while 7 other cases have metastasized (Decree of the Minister of Health of the Republic of Indonesia, 2018).

Prostate cancer can be diagnosed with regular rectal examinations. In the era of PSA (prostate specific-antigen), the diagnosis of prostate cancer patients is usually done about 5-10 years earlier because patients with prostate cancer usually have no symptoms or only show symptoms of disposal and/or storage of urine related to prostate cancer. Significant tools for prostate cancer diagnosis are PSA levels (> 4 ng/ml) and suspicious rectal plug examinations (DRE) (e.g., increased consistency or nodules) (Castillejos-molina and Gabilondo-navarro, 2016). In Indonesia, the most common diagnosis method is biopsy with a total of 57.9% (Decree of the

Minister of Health of the Republic of Indonesia, 2018). A special discovery that usually occurs is the presence of a hard, notched, or rocky channel that is getting bigger. With tumors that are enlarged in the peripheral zone of the prostate, the symptoms resulting from prostatitis are symptoms of sluggishness or as a result of benign prostatic hyperplasia that accompanies it. Hematuria is rare in some cases, but can also occur due to infection or erosion of the glands. Other symptoms include weight loss, bone pain, and neurological complications that can then be seen after metastatic happen on cancer cells (Mazhar and Waxman, 2002).

The risk factors for prostate cancer that can be identified are age, race/ethnicity, and family history related. The first risk factor is age, in the late 1980s, the introduction of prostate-specific antigen (PSA) tests led to a curve in prostate cancer incidence that revealed that the risk of prostate cancer began after the age of 55 and peaked at the age of 70-74 years later decreased thereafter (Gann et al., 1999). Then, another risk factor that can cause prostate cancer is race/ethnicity. Blacks of African descent in the United States had a 58% greater incidence and a 144% higher mortality rate, while Hispanics had a 14% lower incidence and a 17% lower mortality rate compared to whites of European descent (Rawla, 2019). The next risk factor is family or genetic innate factors. The relative risk of developing prostate cancer is higher (RR = 2.48; 95% Cl 2.25-2.74) in men who have first-degree relatives with prostate cancer. This risk is higher in men under the age of 65 (RR = 2.87; 95% CI 2.21–3.74) compared to older men, and if the affected relative is a brother, the risk of getting prostate cancer is (RR = 3.14; 95% CI 2.37–4.15) (Kiciński, Vangronsveld and Nawrot, 2011). Other risk factors that cause prostate cancer are external exposure such as ionic radiation, radiation from ultraviolet light, smoking, food intake, weight, physical activity, and also hormones (Gann et al., 1999).

Prostate cancer can be diagnosed with regular rectal examinations. In the era of PSA (prostate specific-antigen), the diagnosis of prostate cancer patients is usually done about 5-10 years earlier because people with prostate cancer usually have no symptoms or only show mild symptoms related to urination or storage of urine. Commonly used tools for prostate cancer diagnosis are PSA levels (> 4 ng/ml) and suspicious rectal plug (DRE) examinations (e.g., increased consistency or nodules) (Castillejos-molina and Gabilondo-navarro, 2016). The biopsy is the most widely used diagnosis model in Indonesia which is 57.9% of cases (Decree of the Minister of Health of the Republic of Indonesia, 2018). A typical finding that usually occurs is the presence of a hard, grooved, or rocky canal that is growing in size. As the tumor enlarges in the peripheral zone of the prostate, the symptoms due to prostatitis are either slowed down or the result of accompanying benign prostatic hyperplasia. Hematuria is rare in some cases, but it can also occur due to infection or erosion of the glands. Other symptoms include weight loss, bone pain, and neurological complications that can then be seen and associated with metastatic (Mazhar and Waxman, 2002).

Prostate cancer is a disease that develops slowly. There are several treatments that are usually used to treat prostate cancer. Commonly used treatments to treat diseases that are only focused on one part of the body (localized treatment) is active monitoring. A lot of widespread evidence related to cases of low to medium-stage prostate cancer can be done with active monitoring. Its goal is to detect 30% of the most vicious tumors and require further treatment, such as radical prostatectomy (RP) and radiotherapy. However, for some special cases, it takes high-intensity focused ultrasound (HIFU) or cryotherapy, which is a medical procedure to treat tumor cells using a special liquid that can freeze and kill tumor cells. In addition, for post-therapy treatment, hormone blockade is used. This therapy is used to relieve diseases that usually appear after radiation treatment (Castillejos-molina and Gabilondo-navarro, 2016). (Castillejos-molina and Gabilondo-navarro, 2016). The most widely used treatments in Indonesia as a healing effort include 31.1% using orchiectomy, 182 patients (18%) using hormonal drugs, 89 patients (9%) using radical prostatectomy methods, as many as 63 patients (6%) with radiotherapy and the rest using active monitoring, chemotherapy, and combinations (Decree of the Minister of Health of the Republic of Indonesia, 2018). However, in 2005 it was identified that more than 33% of men diagnosed with prostate cancer used some alternative and complementary form, taking at least 25% of their supplement intake, one of which was lycopene (Chen J. et al., 2012).

Tomato fruit has been assumed to be one of the main sources of lycopene production. Fresh tomato fruit has lycopene contents of 30 - 200 mg/kg (Roh et al., 2013), solanine amounted to 0.007 %, saponins, folic acid, malic acid, citric

acid, bioflavonoids (including lycopene, α and ß-carotene), proteins, fats, vitamins, minerals, and histamine (Adams et al., 2004). Lycopene is a tomato carotenoid substance. Lycopene is an acyclic isomer of β-carotene which is a hydrocarbon containing 11 conjugated bonds and 2 unconjugated bonds (Agarwal and Rao, 2000).

Lycopene is one of the most powerful antioxidants (Agarwal and Rao, 2000). Lycopene ability is twice as good as beta-carotene and ten times better than alpha-tocopherol in dampening single oxygen (Kailaku, Dewandari and Sunarmani, 2016). Lycopene is lipophilic and is usually present in cell membranes and other lipid components. Therefore, lycopene has the maximum capability as an anti-reactive oxygen species (Febriansah, Indriyani and Muthi, 2016). In the body, lycopene is necessary as an anticancer substance that serves to fight, slow down and reduce the risk of oxidation. The evidence is that prostate cancer has a low antioxidant content in his blood characterized by increased lipid peroxidation.

Consumption of lycopene may increase the status of lycopene in the body. When ingested, lycopene which has a polyene structure rich in electron systems is broken down into a number of metabolites so that it can react with many free radicals (Tambunan, Nicholas & Umbas, 2015). Lycopene also serves as a blocking agent, where lycopene removes carcinogens from the outside, traps reactive oxygen species, and increases antioxidant potential thereby reducing oxidative damage to lipids (lipoprotein and lipid membranes), proteins (important enzymes) as well as DNA (genetic material). Thus, lycopene can lower oxidative stress. This decrease in oxidative stress can lower the risk of cancer.

As a nonenzymatic antioxidant, lycopene can significantly decrease phase I enzymes (such as cytochrome p450-dependent enzymes) and increase phase II detoxification enzymes (such as hepatic quinone reductase) (Breinholt et al., 2000 in Febriansah, Indriyani and Muthi, 2016). These metabolic enzymes play a role in detoxifying electrophilic compounds that can bind covalently to proteins and nucleic acids. Therefore, cell damage and initiation of mutations can be prevented.

Lycopene also plays a role in protecting important cellular biomolecules, such as lipids, lipoproteins, proteins, and DNA because it blocks the transition in the cell cycle so that it can inhibit the proliferation of cancer cells and induce cell-cycle arrest in the cancer cell line. Thus, important cellular biomolecules can be protected. In healthy human subjects, the lycopene or tomato-free diet caused the loss of lycopene and increased lipid oxidation, while dietary supplementation with lycopene for 1week increased serum lycopene levels and reduced levels of lipid oxidation, protein, lipoprotein, and DNA. Patients with prostate cancer were found to have low lycopene levels and high oxidation rates of serum lipids and proteins (Febriansah, Indriyani and Muthi, 2016).

The phytochemical content in tomatoes is thought to regulate hormones and signaling growth factors in cells. A case-control study conducted with a sample of 112 men showed changes in insulin growth activity – Factor 1 (IGF-1), which stimulates the proliferation of apoptotic resistance in cells. Lycopene supplementation was found to significantly increase the expression of IGF-1 tumors (Novaldy and Iyos, 2016). It is in line with an in vitro experiment conducted by Holzapfel et al. (2013), which showed that tomatoes play a role in decreasing the proliferation and growth of prostate cancer cells. However, this study still showed inconsistent results due to the diversity of lycopene formulations used in the study and differences in research objects (Holzapfel et al., 2013).

According to Tambunan, Nicholas, and Umbas (2015), reinforced by Kailaku, Dewandari and Sunarmani (2016), the bioavailability of lycopene can be higher in processed tomato products such as tomato paste and tomato soup than those derived from fresh tomatoes. In fresh fruit, lycopene is usually available in trans form. Trans form is a form that is not easily absorbed by the body. The lycopene bioavailability properties increase after ripening. It processed tomato products to have more bioavailable-lycopene than fresh tomatoes. Through the processing process, the structure of lycopene cells bound to the trans structure in tomatoes will be detached along with the temperature change and become cis-form to be more easily absorbed by the body (Kailaku, Dewandari and Sunarmani, 2016). It is also in line with research conducted by Soares et al. (2019) that tomato sauce rich in cis-lycopene has a higher bioavailability than trans-lycopene-rich tomato sauce (Soares et al., 2019).

Prospective human studies have found that the consumption of high amounts of lycopene or higher serum lycopene levels may lower the risk of developing prostate cancer (PCa). Dnatural

studies of larger and more comprehensive diets, intake of carotenoids β-carotene, β-carotene, lutein, and β-cryptoxanthin are not associated with the risk of prostate cancer, but high lycopene intake is associated with a 26% decreased risk of prostate cancer (Soares et al., 2019).

Prostate Specific Antigen (PSA) is a glycoprotein produced by epithelial cells lining the asinus and prostate gland ducts. Under normal circumstances, the amount of PSA that enters the bloodstream is only small. However, if there is inflammation or damage to prostate tissue, PSA levels in the blood increase. It is due to the enlargement of the benign prostate, commonly called prostate cancer (Widayati et al., 2013). According to Kailaku, Dewandari, and Sunarmani (2016), in research on prostate cancer patients, lycopene consumption was shown to show a decrease in PSA levels. However, lycopene consumed is a tomato concentrate containing high levels of lycopene. It is in line with other studies contained in Wang et al. (2016) that clinical trials with a sample of 26 patients randomized receiving lycopene supplements 30 mg per day or without supplements. After 3 weeks, patients taking the supplement showed 18% PSA levels with higher prostate lycopene levels. However, Wang et al. (2016) research did not show significant results because it did not have sufficient amounts to check for greater differences in lycopene intake.

CONCLUSION

Prostate cancer is the most common cancer in men in the world after lung cancer. Prostate cancer patients have a low antioxidant content in their blood, increasing oxidation stress and lipid peroxidation. To reduce the risk of oxidation is required to intake antioxidant substances that function as an anticancer substances, one of which is lycopene. Lycopene is one of the most powerful antioxidants, with the ability to dampen single oxygen twice as well as beta-carotene and ten times better than alpha-tocopherol. Although studies conducted on lycopene have not provided clear results, the high antioxidant ability in lycopene can lower oxidative stress so that the risk of prostate cancer also decreases. Increasing the lycopene level can be done by taking lycopene supplements or foods with high lycopene content, such as tomatoes.

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Table 1. Utilization of tomatoes (solanum lycopersicum l.)
To reduce the risk of prostate cancer: a systematic review

Title	Author	Method	Respondents/Samples	Results	Conclusion
A Comparison of Plasma and Prostate Lycopene in Response to Typical Servings of Tomato Soup, Sauce or Juice in Men before Prostatectomy	Elizabeth M. Grainger, Craig W. Hadley, Nancy E. Moran, Kenneth M. Riedl, Michael C. Gong, Kamal Pohar, Steven J. Schwatz, dan Steven K. Clinton.	Experimental Methods	33 men who have been proven by biopsy tests, with 31 having adenocinema in the prostate, 1 having hyperplasia and 1 man having invasive cancer of the bladder, who will undergo prostatectomy.	- It was found that the consumption of tomato soup, tomato sauce, and tomato juice may increase the concentration of prostate lycopene. - With proper calculations, the relationship between lycopene intake and plasma concentrations of lycopene was found to be stronger than epidemiological studies that typically assess intake by FFQ. - However, the correlation between lycopene intake and prostate lycopene concentration or between plasma and prostate lycopene concentration is still rudimentary, which indicates many factors such as food processing, food composition, and genetic/metabolic of the study subjects may affect variations of each individual in lycopene absorption and tissue distribution.	Most processed tomato products can increase plasma concentrations and prostate lycopene in men with prostate cancer in a daily consumption measure within 3 weeks. However, food and biological factors including generics that affect the concentration of lycopene in blood and tissues are not yet known and require more research to clarify the relationship between lycopene and prostate cancer risk.

Antioxidant Effects of Lycopene In African American Men With Prostate Cancer Or Benign Prostate Hyperplasia: A Randomized, Controlled Trial	From Breemen, Richard B. Sharifi, Roohollah Viana, Marlos Pajkovic, Natasha Zhu, Dongwei Yuan, Long Yang, Yanan Bowen, Phyllis E. Stacewicz-Sapuntzakis, Maria	Randomized, double-blind, placebo-controlled study	African-American men aged 50 to 83 with no history of chronic disease, no hypersensitivity to tomato products, and no addiction to **alcohol** or drugs.	- Men who received lycopene for 21 days showed a significant increase in plasma lycopene concentrations compared to the placebo group which was essentially unchanged. - In smokers, there is no significant change in the concentration of plasma lycopene. - In subjects diagnosed with prostate cancer, plasma lycopene concentrations also increased in the lycopene intervention group but not in the placebo group.	Plasma lycopene concentrations **were observed** after lycopene supplementation with lycopene capsules **of** 30 mg/day for 21 days were shown to experience a significant increase, but not in smokers.
Comparative Analysis of Lycopene Content from Different Tomato-Based Food Products on the Cellular Activity of Prostate Cancer Cell Lines	Nathalia da Costa Pereira Soares, Monique de Barros Elias, Clara Lima Machado, Bruno Boquimpani Trindade, Radovan Borojevic and Anderson Junger Teodoro	High Performance Liquid Chromatography (HPLC) Analysis	Tomato-based food products (tomato extract, tomato paste, and tomato sauce) from commercial products at local supermarkets in Rio de Janeiro, Brazil.	Tomato-based food products exhibit strong anti-carcinogenic effects on PC-3 and DU-145 cells. Lycopene obtained from pasta and tomato extract decreases the percentage of PCa cells in phases G0/G1 and G2/M after 96 hours of treatment. However, ketchup and soy sauce extract decreased the percentage of G0/G1 phase cells and increased the percentage of phase S and G2/M cells after a 96-hour treatment.	Lycopene has been shown to be a powerful inhibitor for cell survival, holding cell cycles and improving apoptosis in human prostate cancer cells, showing an effect in the balance of growth of human prostate cancer cell lines
Lycopene, Tomato Products and Prostate Cancer-Specific Mortality	Ying Wang, Eric J. Jacobs, Christina C. Newton and	Prediagnosis dan postdiagnosis dietary	Men of the CPS-II NutritionGroup. After a few exceptions, there were 8,898 prostate	Men diagnosed with non-metastatic prostate cancer, both prediagnosed and post-diagnosed lycopene intake or tomato products are not associated with PCSM.	There was no overall association between lycopene prediagnostic or postdiagnostic diets and

Among Men Diagnosed with Nonmetastatic Prostate Cancer In The Cancer Prevention Study II Nutrition Cohort	Marjorie L. McCullough		cancer patients included in the prediagnosed meal intake analysis and 5,643 included in the postdiagnosed eating intake analysis.	Consistently high lycopene intake afterwards was associated with lower PCSM among men with high-risk prostate cancer but not among men with low-risk prostate cancer	intake of tomato and PCSM products during the long-term follow-up of a large cohort of men diagnosed with nonmetatic prostate cancer.
Serum Lycopene Concentration and Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial	Alan R. Kristal, Cathee Till, Elizabeth A. Platz, Xiaoling Song, Irena B. King, Marian L. Neuhouser, Christine B. Ambrosone, and Ian M. Thomps	Nested Case-Control Study	18,800 men aged about 55 years and above with normal digital rectal examination levels and PSA 3 mg/ml or below and no history of prostate cancer.	Increased serum lycopene in the finasteride group showed a significant decrease in lower-grade cancers only ($P<0.01$, $P = 0.01$, respectively. Meanwhile, in high-level cancers, there is no link between lycopene and prostate cancer risk. In addition, in the placebo group, there was no significant association **between** both lower and upper classes cancers.	The absence of a link between lycopene and the risk of prostate cancer.

The Potential Role of Lycopene for The Prevention And Therapy Of Prostate Cancer: From Molecular Mechanisms To Clinical Evidence.	Wooden Apple, Nina Pauline Wooden Apple, Boris Michael Field, Simon Feldthusen, Jesper Clements, Judith Hutmacher, Dietmar Werner	In vitro and in vivo trials	Bacterium prostatitis and rats	Based on in vitro experiments, the effect of lycopene as protection against prostate cancer cells in the form of **reducing** the risk of reactive oxygen species formation, oxidative **stress-relief,** prevent oxidative DNA damage, drop invasion and migration of tumor cells, **decrease** proliferation and growth of prostate cancer cells. While in vivo experiments showed inconsistent results, caused by the diversity of lycopene formulations and animals used. Some trials showed positive results against decreased prostate cancer and some showed negative results.	In vitro research shows the presence of chemopreventive effects on lycopene on prostate cancer cells, however, its effectiveness in vivo still has to be proven because it shows inconsistent results.