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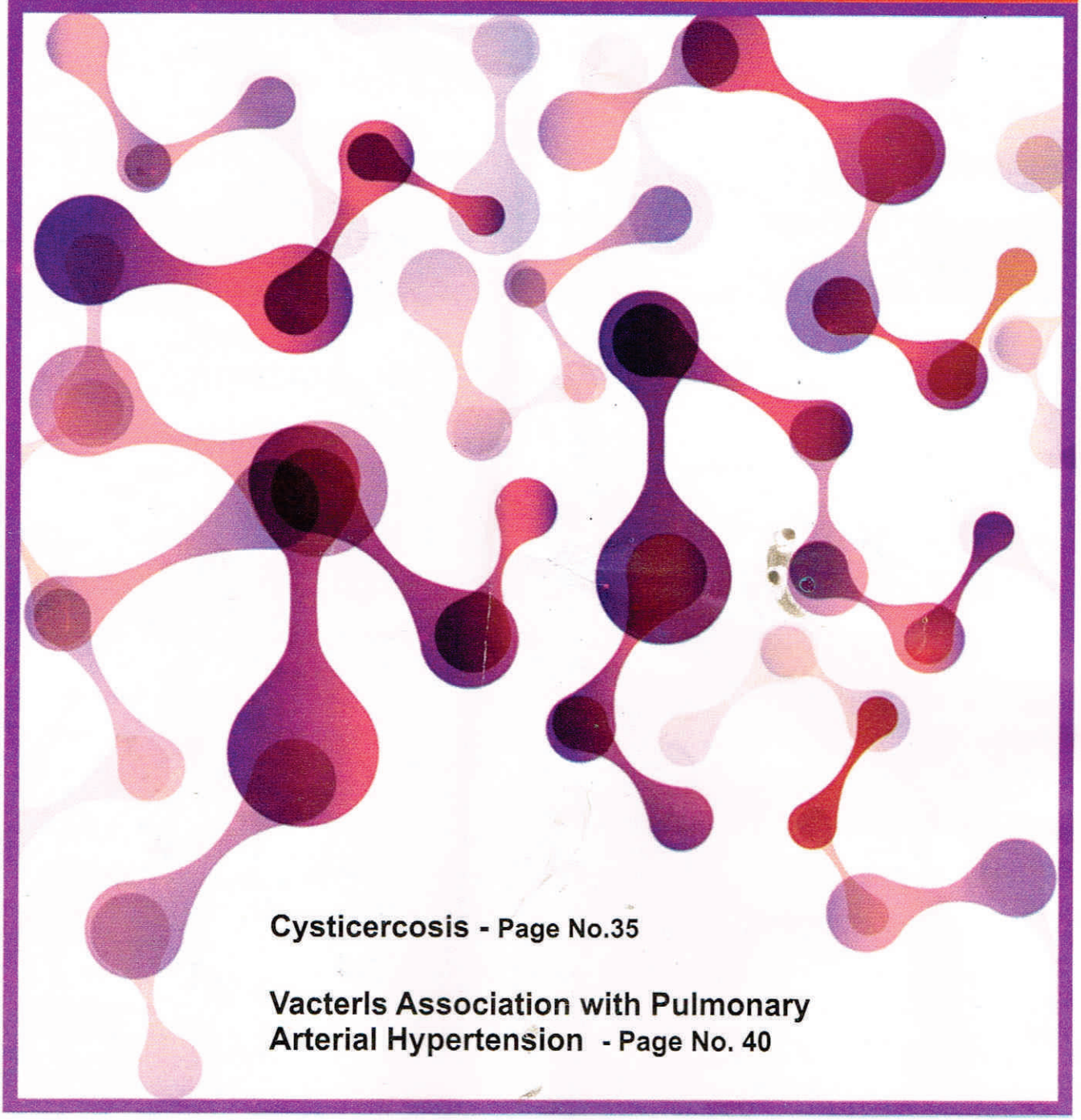

Fate of Lycopene: Splendid Antioxidant to fight against so many Diseases

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Lycopene is a naturally occurring antioxidant that gives fruits and vegetables a red color due to pigment called carotenoids. Lycopene is the most abundant carotenoid in tomatoes with concentrations ranging from 0.9–4.2 mg/100 grams. Other edible sources of lycopene include rosehips, watermelon, papaya, pink grapefruit, and guava.

Lycopene Chemistry

Lycopene is one pigment in a large family of plant pigments known as carotenoids. There are two primary types of carotenoids: hydrocarbon carotenoids and xanthophylls. Hydrocarbon carotenoids, such as lycopene, are composed entirely of hydrogen and carbon. In contrast, xanthophylls, such as lutein, contain oxygen in addition to carbon and hydrogen[5]. The chemical formula for lycopene is C40H56. The 11 conjugated and 2 unconjugated double bonds present in lycopene allow for extensive isomerization, resulting in 1056 theoretical cis-trans configurations[6]. Only a few isomers are actually found in nature, however, [Figure 1] with the all-trans configuration of lycopene being the most common isomer found in foods[7].

Figure 1.

Oxidative Stress & Lycopene

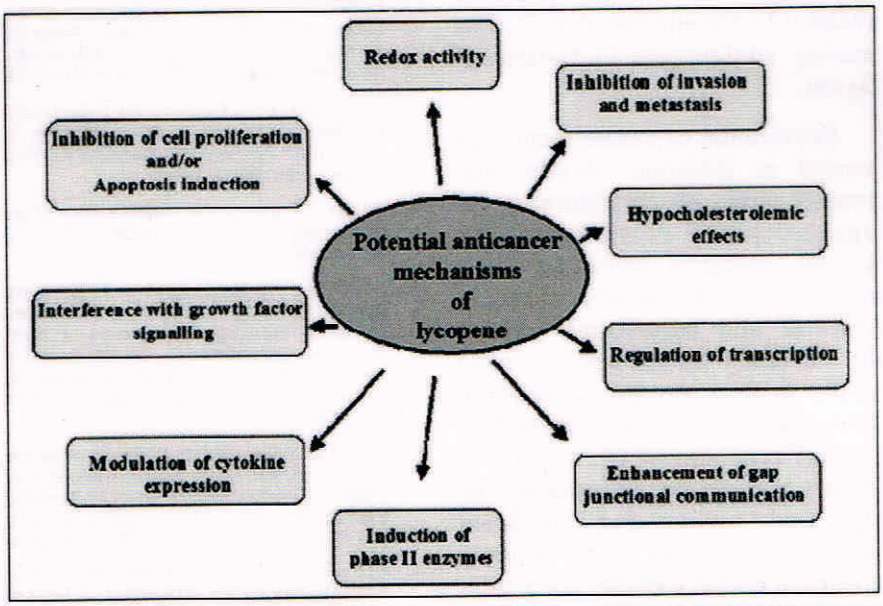
Reactive oxygen species (ROS) are oxygen-containing molecules that either are or have the potential to generate free radicals. Overproduction of ROS results in a condition known as oxidative stress, which has been linked to both cancer and cardiovascular disease. Carotenoids, including lycopene, can be potent antioxidant molecules and are especially effective at scavenging the ROS singlet oxygen. The extended conjugated polyene chain of lycopene is an electron-rich system, susceptible to attack by electrophilic reagents. Therefore, carotenoids like lycopene are unstable and highly reactive towards oxygen and free radicals[8]. This reactivity of lycopene is the basis for its anti-oxidant activity in biological systems that might contribute to its efficacy as a chemoprevention agent.

Figure 1. Lycopene Chemical Structure

Lycopene bioavailability

Bioavailability can be affected by a number of factors, including food processing and dietary composition. Thermal processing generally improves lycopene bioavailability by disrupting cellular membranes, which allows lycopene to be released from the tissue matrix[9]. Multiple studies have shown that lycopene from thermally processed tomato products is more bioavailable than lycopene from fresh tomatoes[10]. Lycopene bioavailability is greatly affected by dietary composition. Given that lycopene is a lipid-soluble compound, consuming it with fat increases its bioavailability. Human organs store lycopene to varying degrees. Lycopene is found in the highest concentrations in the liver, testes, adrenal glands, and adipose tissues[11]. It is found in lower concentrations in the kidney, ovary, lung, and prostate[11].

Mechanisms of Cancer Prevention by Lycopene



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1. Redox Activity

   Oxidative stress is recognized as one of the major contributors to the increased risk of cancer. The system of conjugated double bonds allows lycopene molecule to efficiently quench the energy from very deleterious forms of oxygen (singlet oxygen) and to scavenge a large spectrum of free radicals. Lycopene has been reported to deactivate in vitro an array of free radicals, such as hydrogen peroxide, nitrogen dioxide, thyl, and sulphonyl[12]. There are a number of investigations demonstrating in vitro that lycopene is a more potent ROS scavenger than many other dietary carotenoids and other antioxidants, including vitamin E.

2. Inhibition of Cancer Cell Proliferation and Apoptosis Induction

   The inhibitory effects of lycopene have been accompanied by inhibition of cell cycle progression from the G0/G1 to the S phase[13] and by changes in proteins controlling cell cycle. In particular, lycopene has been reported to decrease cyclin D1 and to increase p53.

3. Interference with Growth Factors Stimulation of Cancer Cell Proliferation

   IGF-1-stimulated cell growths, as well as DNA binding activity of the AP-1 transcription factor, were reduced by physiological concentrations of lycopene in endometrial, mammary, and lung cancer cell lines. In such models, lycopene was able to inhibit IGF-1-stimulated insulin receptor substrate 1 phosphorylation and cyclin D1 expression, to block IGF-1-stimulated cell cycle progression[14].

4. Cancer Prevention by Inducing Phase II Enzymes

   Rise in the level of reduced glutathione, enzymes of the glutathione redox cycle, and glutathione S-transferase (GST)

5. Regulation of Transcription

   Lycopene modulates the basic mechanisms of cell proliferation, growth factor signaling, and gap junctionalintercellular communication [15].

6. Hypocholesterolemic Effects

   Lycopene dose-dependently reduced intracellular total cholesterol by decreasing 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase expression[16].

7. Modulation of Cytokine Expression

   Pro-inflammatory cytokines, such as interleukins (ILs) and tumor necrosis factor-alpha (TNF-α), have been implicated in tumor promotion in various experimental models of tumor genesis. Lycopene reduces these cytokines level.

Lycopene & Animal study

Multiple animal models including rats, mice and ferrets, have been used to explore the efficacy of lycopene in the prevention of cancer in various tissues. Since the strongest clinical evidence for the benefits of lycopene in cancer are for prostate cancer chemoprevention, the majority of animal studies with lycopene have concerned prostate cancer. Smoke exposure decreased the elevated lycopene concentrations in plasma and lung tissue of ferrets supplemented with lycopene, which is consistent with the data from National Health and Nutrition Examination Survey III that has found that smokers had lower serum level of lycopene compared with non-smokers[17]. Both low- and high-dose lycopene supplementations substantially inhibited smoke-induced squamous metaplasia and proliferating cell nuclear antigen (PCNA) expression in the lungs of ferrets[17]. No squamous metaplasia or PCNA overexpression was found in the lungs of control ferrets or those supplemented with lycopene alone. Ferrets supplemented with lycopene and exposed to smoke had significantly higher plasma insulin growth factor binding protein 3 (IGFBP-3) levels and a lower insulin growth factor-1 (IGF-1)/IGFBP-3 ratio than ferrets exposed to smoke alone. In a recent issue of The Journal of Nutrition, Huang et al.[18] reported that lycopene inhibits experimental metastasis of human hepatoma SK-Hep-1 cells in athymic nude mice. In that study, lycopene or β-carotene-treated mice were injected with human hepatoma SK-Hep-1 cells via the tail vein. At the end of the experiment, lycopene-treated mice had a lower number of tumors and decreased tumor cross-sectional areas in the lung than the control mice. Lycopene treatment also decreased the rate of proliferating cell nuclear antigen, level of vascular endothelial growth factor, and protein expression of proliferating cell nuclear antigen, level of vascular endothelial growth factor, and metalloproteinase. Similar results were found in mice treated with β-carotene. Based on the data presented, β-carotene appears to be more effective than lycopene in attenuating the lung metastasis and related indices examined.

Lycopene - Potential Health Benefits& Clinical study

Cancer

Of the diseases studied in relation to lycopene, prostate cancer is one of the best researched. In addition to prostate cancer, benign prostatic hyperplasia (BPH), the age related

non-cancerous overgrowth of the prostate gland, also negatively affects men's health. Intake of ≥2 servings of tomato sauce per week was associated with a reduced risk of prostate cancer [relative risk (RR) = 0.77 relative to <1 serving of tomato sauce per month, Ptrend <0.001]. Lycopene intake was also associated with a reduced risk of prostate cancer, but the association was weaker[19]. A recent meta-analysis demonstrated a modest inverse relationship between intake of raw tomatoes (RR = 0.89 for highest versus lowest quartile of intake) and tomato products (RR = 0.81 for highest versus lowest quartile of intake) and prostate cancer[20].

Two case-control studies comparing the dietary habits of women with and without breast cancer also observed a significant decrease in the odds ratio of those who consumed the highest amount versus the lowest amount of dietary lycopene[21].

Epidemiological studies suggest that higher intake of lycopene is associated with either a reduced risk of lung cancer[22], or no change in lung cancer risk, as compared with lower intake levels.

In a prospective cohort study of 3182 free living subjects in rural Japan, higher serum levels of lycopene were significantly associatedwith a reduced risk of colorectal cancer mortality[23].

Cardiovascular Diseases

Increasedplasma lycopene levels have been associated with reductions in CVD risk and have also been reported to improve biomarkers associated with CVD. For example, a study by Sessoet al. (2003) of 38,445 women found that higher levels of tomato-based product intake were associated with a reduced risk of cardiovascular disease (RR = 0.71, Ptrend= 0.029) and myocardial infarction (RR = 0.43, Ptrend = 0.033) between the highest and lowest quintiles of intake[24].

Some studies have shown that lycopene may reduce cholesterol synthesis and increase low-density lipoprotein (LDL) degradation[25]. A randomized crossover study by Agarwal&Rao (1998) used four different treatments: placebo (0 mg lycopene), tomato juice (50.4 mg lycopene), spaghetti sauce (39.2 mg lycopene), and tomato oleoresin (75 mg lycopene). Nineteen healthy subjects consumed each treatment daily for one week and went through a one week washout period between each treatment week. Serum lycopene concentration doubled in subjects on the lycopene containing treatments. In addition, a significant decrease in serum lipid peroxidation and LDL oxidation was observed after subjects consumed any one of the three lycopene containing treatments[26].

Other diseases (Evidence Level C – Unclear Scientific Evidence for below Mentioning Conditions)

Asthma

Blood thinner

Brain tumors

Type 2 Diabetes

Eye disorders

Gum diseases

High blood pressure

High blood pressure associated with pregnancy

Infertility

Menopause

Dosing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven.

Adults (18 years and older)

Many available studies have looked at the effects of mixed-ingredient therapies that contain lycopene. According to the manufacturer, these two supplements contain lycopene and other nutrients found in whole tomatoes.

As an antioxidant, lycopene has been taken by mouth in doses of 6.5, 15, and 30 milligrams daily for eight weeks. 15 milligrams have been taken by mouth once daily for eight weeks and 26 days, or twice daily for four months. Two capsules (each capsule containing 15 milligrams of lycopene) have been taken by mouth once daily for 21 days.

To treat asthma caused by exercise, 30 milligrams of lycopene has been taken by mouth daily for one week.

To treat coronary artery disease, 1.24 grams of six-percent lycopene oleoresin capsules has been taken by mouth daily for one week. Two softules (each containing 2,000 micrograms of lycopene) have been taken by mouth daily for six months. Lycopene has been taken by mouth in the form of tomato products, capsules, in doses of 39.2-80 milligrams for 1-12 weeks.

To treat enlarged prostate, 15 milligrams of lycopene has been taken by mouth daily for six months.

To treat brain tumors, eight milligrams of lycopene has been taken by mouth daily for three months.

To treat heart disease, lycopene has been taken by mouth in the form of tomato products, capsules, in doses of 39.2-80 milligram doses daily for 1-12 weeks.

To treat gum disease, eight milligrams of lycopene has been taken by mouth daily in divided doses for two weeks.

To treat high blood pressure, lycopene has been taken by mouth in 4-44-milligram doses daily for up to six months. 15 milligrams of lycopene, has been taken by mouth daily for six weeks and eight weeks. A dose of 250 milligrams of Lycopene has been taken by mouth for eight weeks.

To treat infertility, 2,000 micrograms of lycopene has been taken by mouth twice daily for three months.

To lower lipid levels, lycopene has been taken by mouth in 4-44-milligram doses daily for up to six months. Two softules (each containing 2,000 micrograms of lycopene) have been taken by mouth daily for six months.

To treat mouth sores, 4-8 milligrams of lycopene, has been taken by mouth daily for three months in two divided doses.

To treat inflammation of the mouth, 16 milligrams of lycopene has been taken by mouth daily in two divided doses for two months.

To prevent ovarian cancer, 4,000 micrograms of lycopene has been taken by mouth daily.

To treat high blood pressure associated with pregnancy, two milligrams of lycopene per capsule has been taken once or twice daily until delivery.

To prevent or treat prostate cancer, two milligrams of lycopene has been taken by mouth twice daily, and four milligrams of lycopene has been taken by mouth twice daily for one year. 120 milligrams of lycopene, has also been taken by mouth in divided doses twice daily for periods of up to one year. Softules, providing a total daily dose of 10 milligrams of lycopene, have been taken daily for three months.

To protect skin from Sun damage, 55 grams of tomato paste in olive oil (providing 16 milligrams of lycopene) has been taken by mouth daily for 12 weeks.

Children (younger than 18 years)

There is no proven safe or effective dose for lycopene in children.

Side Effects and Warnings

There is not enough evidence at this time on the safety of lycopene supplements.

Use cautiously in people who have stomach ulcers or other stomach problems, or those taking stomach agents.

Hypotension

Increase the risk of bleeding

Use cautiously in people who are taking estrogen, estrogen-like compounds, or other hormone therapy. Lycopene may interact with isoflavones.

Lycopene may interfere with tests for prostate cancer.

Avoid in children and in pregnant or breastfeeding women, due to a lack of safety information.

Avoid in people who are allergic or sensitive to lycopene, tomatoes, or other ingredients in lycopene-containing supplements.

Lycopene may also cause anorexia, chest pain, diarrhea, fat buildup under the skin, feeling of pressure in stomach, gassiness, heart attack, indigestion, nausea, skin discoloration, stomach pain, stomach ulcer irritation, vomiting, and worsened hot flashes.

Pregnancy and Breastfeeding

There is a lack of scientific evidence on the use of lycopene during pregnancy or breastfeeding.

Interactions

Interactions with Drugs

Lycopene may increase the risk of bleeding when taken with drugs that increase the risk of bleeding. Some examples include aspirin, anticoagulants (blood thinners) such as warfarin (Coumadin®) or heparin, antiplatelet drugs such as clopidogrel (Plavix®), and nonsteroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®).

Lycopene may cause low blood pressure. Caution is advised in people taking drugs that lower blood pressure.

Conclusion

This papeis showing lycopene chemistry, sources, intake, bioavailability, and recent data regarding the potential health effects of lycopene. Discrepancies between animal data, which are generally more positive than human data, which are less clear, may be due to differences in carotenoid absorption and metabolism in humans relative to other species as well as inter-individual differences in humans. Animal studies are typically conducted using inbred animals, reducing genetic variability and producing clearer results. Lycopene's effects may vary from person to person based on dietary lycopene and fat intake, probiotics, genetic differences in metabolism, and other factors.

Lycopene does having significant effects on so many diseases in humans with varied mechanism; still awareness among physicians and patients is not up to that extreme. Many case-control and cohort studies have examined lycopene-rich diets and various cancers, suggesting there is astrong role of lycopene in preventing cancers. Lycopene almost showed as promising results as other antioxidants like Vitamin E, Vitamin C. Though more numbers of very well organized clinical trials are required to prognosticate lycopene, main limitation of lesser use of this antioxidant in Indian people is knowledge which should be mainly delivered by physicians. This issue should be well addressed to both physicians and patient's level.

It is only through such studies that our understanding of the anticancer role played by tomato lycopene will be enhanced and help us to develop complementary strategies for the prevention, treatment and management of lung cancer.

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Chest pain is the most common complaint in the emergency department (ED) globally. A large number of patients hospitalized for the clinical suspicion of acute coronary syndrome (ACS); however, diagnosis is confirmed in only some of them. Patients who are admitted to EB with chest pain are suggestive of ACS have considerable clinical symptoms overlap with those who present with non-cardiac chest pain.

The most used scale to patients with stratify chest pain are thrombolysis in myocardial infarction (TIMI) score with other like history, electrocardiogram, age, risk factors, and troponin (Heart), global registry of acute coronary events (Grace) and branch scores. However, these methods are not validated to determine who has ACS.

- CVD Times