International Journal of Medical and Pharmaceutical Sciences
Open access peer-reviewed Journal
Volume 2, Issue 4, Page 13-20.
https://doi.org/10.5281/zenodo.19771348

Review Article

Lycopene: A Comprehensive Review of Sources, Extraction, Bioavailability, Pharmacological Activities and Future Perspectives

Praveen Kumar Pal[1], Minakshi[2], Abhishek Singh[3], Pradeep Kumar[4]

[1]*Department of pharmacy, [CH. SUGHAR SINGH PHARMACY COLLEGE][Jaswantnagar, Etawah]*
[2]*Department of pharmacology, [CH. SUGHAR SINGH PHARMACY COLLEGE][Jaswantnagar, Etawah]*
[3]*Department of pharmaceutis, [CH. SUGHAR SINGH PHARMACY COLLEGE][Jaswantnagar, Etawah]*
[4]*Department of pharmaceutical Chemistry, [CH. SUGHAR SINGH PHARMACY COLLEGE][Jaswantnagar, Etawah]*

A naturally occurring pigment called lycopene gives tomatoes, watermelon, papaya, guava, and several other fruits their red hue. Among dietary carotenoids, it is one of the most effective singlet oxygen quenchers due to its highly conjugated double-bond structure, which also confers significant antioxidant qualities. Because of its potential to lower the risk of chronic diseases linked to oxidative stress, such as cardiovascular disorders, diabetes, neurodegenerative diseases, and skin aging, lycopene has garnered a lot of scientific and clinical attention over the past 20 years. In addition to its physiological uses, lycopene is frequently used as a natural food coloring, nutraceutical ingredient, and functional additive in pharmaceutical and cosmetic compositions. With a focus on (i) natural sources and chemistry, (ii) extraction and analytical methods, (iii) bioavailability and metabolism, (iv) pharmacological activities backed by experimental and clinical data, and (v) industrial applications, this review offers a thorough analysis of lycopene. Additionally, future views that include delivery techniques based on nanotechnology and sustainable biotechnological production are examined, along with the difficulties related to stability, poor bioavailability, and unpredictability in human reaction. All things considered, the evidence suggests that lycopene has great potential as a preventative and therapeutic agent; however, to reach its full clinical and commercial potential, extensive randomized clinical studies and standardized safety evaluations are still necessary.

Keywords: Lycopene; Antioxidant; Bioavailability; Pharmacological activities; Functional foods; Cis-isomers; Oxidative stress.

INTRODUCTION

Natural antioxidants have gained significant attention due to their important role in maintaining human health and preventing various chronic diseases. Oxidative stress, caused by the excessive production of reactive oxygen species (ROS), is a major factor involved in the development of cardiovascular diseases, cancer, diabetes, and other disorders. Unhealthy dietary habits further contribute to this imbalance, increasing the need for natural compounds that can reduce oxidative damage. Plant-based bioactive compounds are widely recognized for their therapeutic potential. These natural products, including polyphenols, carotenoids, and vitamins, act as antioxidants by neutralizing free radicals and protecting cellular components. Among these, lycopene is an important carotenoid known for its strong antioxidant properties.

Lycopene is a lipophilic pigment responsible for the red color of fruits and vegetables such as tomatoes, watermelon, papaya, and pink grapefruit. It has a unique chemical structure with multiple conjugated double bonds, which contribute to its high free radical scavenging ability. Unlike some other carotenoids, lycopene does not have provitamin A activity but shows significant health benefits.

Several studies have suggested that lycopene plays a protective role against chronic diseases, including cardiovascular disorders and certain types of cancer. It also exhibits anti-inflammatory and antioxidant activities, which help in reducing oxidative stress. However, its bioavailability is influenced by factors such as food processing, isomerization, and dietary composition.

In addition to its health benefits, lycopene is also used as a natural antioxidant in food systems to improve stability and shelf life by preventing lipid oxidation. Due to safety concerns associated with synthetic antioxidants, lycopene is considered a safer alternative.

Overall, lycopene is a promising natural compound with potential applications in food, pharmaceutical, and nutraceutical industries. This review focuses on its sources, extraction methods, bioavailability, pharmacological activities, and future perspectives.

2. Sources and Chemistry of Lycopene-

2.1 Natural Sources:

Lycopene is found in a wide variety of foods, mostly in fruits and vegetables that are red or pink in color. In the majority of populations, tomatoes and tomato-derived products (juice, paste, ketchup, and puree) continue to be the main nutritional source, making up between 80 and 85 percent of total intake. Depending on the cultivar, ripening stage, and environmental factors, fresh tomatoes can have lycopene concentrations ranging from 8 to 42 mg/kg.

Additional significant sources include of:

With concentrations ranging from 23 to 72 mg/kg, watermelon (Citrullus lanatus) is a rich non-tomato source.

Lycopene levels in pink guava (Psidium guajava) range from 54 to 70 mg/kg.

Papaya (Carica papaya): Provides 20–50 milligrams per kilogram.

Red bell peppers (Capsicum annuum): Less important as a dietary contributor, yet up to 20 mg/kg.

Moderate levels are provided by grapefruit (Citrus paradisi, pink/red varieties).

2.2 Chemical Structure -

Lycopene has a molecular weight of 536.9 g/mol and is an acyclic carotenoid made up of 40 carbon atoms ($C_{40}H_{56}$). Its linear polyene chain, which has two unconjugated and eleven conjugated double bonds, defines its structure. The following are the main causes of these conjugated double bonds:

Color: Deep red coloring is produced by strong absorption in the visible range (470–510 nm).

Reactivity: Resonance stabilization gives it a high antioxidant potential.

2.3 Isomeric Forms -

In raw plant materials, lycopene is primarily found in the all-trans configuration. Nevertheless, isomerization is induced by heating, processing, and acidic conditions, resulting in cis-isomers. Cis-isomers show improved solubility in micelles of bile salt.

increased gut cell absorption efficiency.

Human bioavailability is higher than that of the all-trans form.

Research has indicated that whereas tomatoes mostly contain all-trans lycopene, over 50% of the circulating plasma lycopene in people is in cis form.

2.4 Stability Issues -

Lycopene is highly sensitive to external factors such as:

Heat: Prolonged heating leads to degradation.

Light: Exposure to UV accelerates oxidative breakdown.

Oxygen: Auto-oxidation produces epoxides and other degradation products.

Therefore, appropriate storage and packaging conditions (dark, oxygen-free, and cool environments) are crucial to preserve lycopene integrity in foods and supplements.

3.1 Conventional Solvent Extraction:

Hexane, acetone, ethanol, and petroleum ether are examples of organic solvents that have been used historically to extract lycopene. The procedure includes filtration, solvent extraction, solvent evaporation, and homogenization of the plant material.
Benefits include simplicity and a high yield.

Limitations include low selectivity, hazardous solvents, and environmental issues.

3.2 Advanced and Eco-Friendly Extraction Methods -

Supercritical Fluid Extraction (SFE): -Uses supercritical CO_2 as a solvent, frequently in combination with ethanol.

-Provides solvent-free extracts, excellent purity, and selectivity.
-Environmentally friendly, but expensive for widespread use.
Ultrasound-Assisted Extraction (UAE): -Disturbs plant tissues by use of acoustic cavitation.
-Decreases time and solvent usage while improving mass transfer.
-Microwave-Assisted Extraction (MAE): -The heating of plant tissues is accelerated by microwave energy.
-Improves efficiency and yield in comparison to traditional approaches.
-Enzyme-Assisted Extraction: -Uses enzymes that break down cell walls, such as pectinase and cellulase, to increase the release of lycopene.
-Improves extraction efficiency, particularly in the value-adding of tomato waste.

3.3 Chromatography and Spectrophotometric Analysis:

High-Performance Liquid Chromatography (HPLC):
· The most reliable method for measuring lycopene, frequently used in conjunction with UV-Vis or detectors used in mass spectroscopy.
Although less precise than HPLC, ultraviolet-visible (UV-Vis) spectroscopy is useful for quick quantification. Liquid Chromatography-Mass Spectrometry (LC-MS) offers in-depth examination of lycopene isomers and degradation products.

3.4 Industrial Applications of Extraction:

One of the main sources of lycopene extraction used by the food industry is tomato pomace, or processing waste, which provides a cost-effective and sustainable method. In order to reduce environmental effect and guarantee consumer safety, green extraction process optimization is becoming more and more important.

4.1 Mechanism of Absorption:

As a lipophilic carotenoid, lycopene is absorbed in the small intestine by pathways that resemble those of dietary lipids. Release from the food matrix during digestion is the first step in the process.

incorporation into lipid micelles made possible by dietary fats and bile salts.
passive diffusion and facilitated transport (e.g., scavenger receptor class B type I, SR-BI) by enterocytes.

4.2 Elements That Affect Bioavailability

Food matrix and processing: Because of heat isomerization, lycopene from processed tomato products (paste, juice, and sauce) is more accessible than from raw tomatoes.
Isomeric form: All-trans lycopene is not as well absorbed as cis-lycopene is.

Dietary fat: Promotes the synthesis and absorption of micelles.
Genetic variability: The efficiency of lycopene absorption is impacted by polymorphisms in genes such as SCARB1 and CD36.
Age and health: Patients with gastrointestinal issues and the elderly frequently have decreased absorption.
Interactions with other carotenoids: Lycopene absorption may be competitively inhibited by a high consumption of β-carotene. joining chylomicrons to be carried into circulation via the lymphatic system. Dietary fat is essential for the absorption of lycopene, and consuming it with foods high in oil greatly increases its bioavailability.

4.3 Distribution and Metabolism:

Chylomicrons, VLDL, LDL, and HDL fractions are the vehicles in which lycopene is transported after absorption. It mainly builds up in the testes, liver, and adrenal glands (highest concentrations).

-Skin and prostate (indicating functions in photoprotection and disease prevention). One long-term storage location is adipose tissue.Apo-lycopenals, apo-lycopenols, and apo-lycopenoic acids are among the metabolites that are produced during metabolism by enzymatic cleavage routes. It is thought that these metabolites have unique biological properties, such as modifying nuclear receptors (retinoid X receptor, for example).

4.4 Elimination:

There is little excretion of lycopene and its metabolites in the urine; instead, they are mainly eliminated through bile into feces. Based on dietary intake and metabolic rate, lycopene has a biological half-life of 5 to 9 days.

4.5 Bioavailability Issues -

Lycopene has issues despite its potential to improve health:
Inadequate solubility in water.

-A resistance to oxygen, heat, and light.
-Differing individual absorption efficiency.
"-"To get over these obstacles, researchers are looking into novel delivery methods such solid lipid nanoparticles, liposomes, nanoemulsions, and biopolymer complexes.

5.1 Antioxidant and Anti-Inflammatory Properties:

Lycopene is regarded as one of the strongest antioxidants found in food. It effectively scavenges hydroxyl radicals, superoxide anions, and singlet oxygen thanks to its conjugated double-bond structure.
Lycopene has a quenching rate constant of approximately $31 \times 10^9\ M^{-1}\ s^{-1}$, which is higher than that of other carotenoids. A crucial stage in atherosclerosis, oxidative alteration of LDL is prevented by lipid peroxidation inhibition. Transcription factor modification reduces pro-inflammatory cytokines and increases the expression of antioxidant enzymes by suppressing NF-κB activation and improving Nrf2 signaling.

5.2 Protective Effects on the Heart:

Consuming lycopene has been associated with better cardiovascular health in a number of observational studies and clinical trials.
Modification of the lipid profile: Lycopene lowers LDL and total cholesterol while somewhat raising HDL.

Blood pressure control: It has been demonstrated that taking supplements of lycopene (15–30 mg/day) lowers both the systolic and diastolic blood pressure.
Endothelial function: Promotes vascular relaxation by increasing nitric oxide bioavailability.
Clinical evidence: Lycopene supplementation dramatically lowers systolic blood pressure in hypertensive individuals, according to a meta-analysis of randomized controlled trials.

5.3 Epidemiologic evidence of anticancer activity:

Reduced chances of stomach, lung, and prostate cancers are inversely correlated with high consumption of tomatoes and lycopene.

Strong preventive benefits against prostate cancer, particularly aggressive types, are highlighted by prospective cohort studies.
Molecular Processes
Cell cycle regulation: At the G_0/G_1 phase, lycopene causes cell cycle arrest.
Pro-apoptotic proteins (Bax) are enhanced while anti-apoptotic proteins (Bcl-2) are suppressed during apoptosis induction.
Growth signaling inhibition: stops the excessive IGF-1 signaling pathway that is frequently seen in malignancy.
Epigenetic modulation: Modifies the patterns of histone acetylation and DNA methylation in tumor cells.
Clinical and Preclinical Research
In models of prostate cancer, lycopene

supplementation has been proven to slow the growth of tumors.
Prostate cancer patients who take supplements containing tomatoes have shown lower PSA levels in several clinical trials.

5.4 Neuroprotective Effects:

The core causes of neurodegenerative illnesses like Parkinson's and Alzheimer's are oxidative stress and neuroinflammation.
preclinical results: Lycopene attenuates dopaminergic neuronal loss, lowers neuroinflammation, and lessens oxidative damage caused by amyloid-β.

Mechanisms include modulating apoptotic signaling, reducing ROS generation, and suppressing microglial activation.
Cognitive function: Lycopene supplementation enhances memory and learning in animal models. There is little, but encouraging, human evidence that greater plasma lycopene levels are associated with a lower incidence of dementia and cognitive decline.

5.5 Anti-metabolic and Anti-diabetic Effects:

Insulin secretion is enhanced when oxidative stress is reduced in pancreatic β-cells.
Glycemic control: Preclinical research shows that supplements lower fasting blood glucose and HbA1c levels.

Lipid metabolism lowers the risk of metabolic syndrome by improving triglyceride and cholesterol levels.
anti-inflammatory effects: TNF-α and IL-6, which are increased in diabetes, are downregulated.

5.6 Impact on Dermatology and Photoprotection:

Lycopene helps prevent skin from UV ray damage and promotes skin health.
Photoprotection: After being exposed to UV light, oral supplements lessen the production of erythema.
Preserving collagen delays the creation of wrinkles by preventing oxidative damage to skin proteins.
Hydration and suppleness of the skin: formulations enhanced with lycopene enhance the function of the skin barrier.
Cosmetic use: Often found in oral nutraceuticals and anti-aging treatments for healthy skin.

5.7 Additional Biological Impacts:

Osteoporosis risk is decreased and bone mineral density is increased when lycopene intake is increased.
Lycopene enhances sperm motility and lessens oxidative DNA damage in spermatozoa, which benefits male reproductive health.

Immune modulation: Boosts the immune system's overall response and increases the activity of natural killer cells.

6.1 Food Industry:

-Lycopene is a natural pigment (E160d) that is widely utilized in the culinary sector to give liquids, sauces, ketchup, dairy products, and candies their red hue. Because it provides more nutritional and health-promoting advantages than synthetic hues, lycopene is a desirable ingredient in functional meals. Sports drinks, nutritional supplements, and juices enhanced with lycopene are examples of functional foods and beverages that are being promoted more and more. Lipid oxidation can be prevented by lycopene's antioxidant action, which can improve food stability.

6.2 Industry for Nutraceuticals:

Typically, lycopene dosages range from 5 to 30 mg per day and are available as dietary supplements in the form of capsules, soft gel, and powder. AAntioxidant blends frequently include formulations that combine vitamin C, vitamin E, selenium, and polyphenols.

-Prostate and cardiovascular health, skin protection, and overall antioxidant support are the main topics of health claims.

6.3 Use in Cosmetics and Pharmaceuticals:

Drugs: Formulations enhanced with lycopene are created to treat prostate issues, hypertension, and hyperlipidemia levels

Cosmetics and Dermatology: Lycopene is used in oral nutricosmetics, anti-aging lotions, and sunscreens. Clinical research backs up its skin-rejuvenating and photoprotective benefits.
As a supplemental treatment for breast and prostate cancers, lycopene supplementation is being researched as a cancer adjuvant.

6.4 Applications in Biotechnology and Agriculture:

Pomace from tomato processing: An environmentally friendly source of raw materials for the production of lycopene.
Biotechnological production: Lycopene is intended to be produced through fermentation with the use of E. coli and Saccharomyces cerevisiae in microbial engineering advancements. Encapsulation technologies: For commercial-scale fortification, biopolymers, nanoemulsions, and lipid carriers are being investigated.

7.1 Storage and Stability:

Lycopene is extremely unstable when exposed to heat, light, and oxygen. This makes large-scale manufacture and storage more difficult and shortens its shelf life. Refrigeration, encapsulation, and protective packaging are essential.

7.2 Issues with Bioavailability:

Lycopene has a low oral bioavailability because it is hydrophobic, even though it has a great antioxidant potential. Active development is underway for strategies including emulsification, lipid-based carriers, and nanoparticle delivery.

7.3 Human Response Variability:

Genetic variations in transport and absorption proteins (such SCARB1) lead to inter-individual variations in plasma lycopene levels, which makes it more difficult to develop dietary guidelines that apply to everyone.

7.4 Regulatory and Safety Aspects:

Although lycopene is permitted as a food additive by EFSA and is classified as Generally Recognized as Safe (GRAS) by the FDA, the lack of uniform dose

Therapeutic usage standards continue to be a barrier.

7.5 Topics for Future Research and Additional Study:

• Extensive, randomly assigned clinical investigations are desperately needed to identify therapy advantages unique to distinct disorders.

• Research on the unique biological roles of lycopene metabolites, like apo-lycopenals and apo-lycopenoic acids, is necessary.

• It is crucial to develop biotechnology-based, environmentally friendly manufacturing techniques in addition to improving agricultural and industrial waste materials.

• These findings must be incorporated into customized nutrition regimens and preventative healthcare strategies.

CONCLUSION

Lycopene is a potent carotenoid distinguished by its significant antioxidant and anti-inflammatory properties, which contribute substantially to the prevention and management of chronic diseases, including cardiovascular disorders, various malignancies, diabetes, neurodegenerative conditions, and cutaneous aging. Beyond its therapeutic potential, lycopene has garnered increasing attention across multiple industries, including the food sector, nutraceuticals, pharmaceutical formulations, and cosmeceuticals. Nevertheless, several limitations persist, such as its chemical instability, poor bioavailability, and interindividual variability in physiological response, which hinder its optimal utilization.

Recent advancements in nanotechnology, biotechnology, and biomedical research present promising strategies to enhance lycopene delivery systems and to establish standardized dosing protocols. With continued scientific investigation and technological innovation, lycopene is poised to emerge as a key bioactive compound in functional foods, nutraceutical products, and evidence-based preventive healthcare inventions.

REFERENCES

1. Arballo J, Amengual J, Erdman JW Jr. Lycopene: A critical review of digestion, absorption, metabolism, and excretion. Antioxidants. 2021;10(3):342.
2. Przybylska S. Lycopene – a bioactive carotenoid .offering multiple health benefits: a review. Int J Food Sci Technol. 2020;55(1):11-32.
3. Chen J, Song Y, Zhang L. Lycopene/tomato consumption and the risk of prostate cancer: A systematic review and meta-analysis. Nutr Cancer. 2013;65(6): 881-896.
4. Cheng HM, Koutsidis G, Lodge JK, Ashor A, Siervo M, Lara J. Lycopene and tomato and risk of cardiovascular diseases: A systematic review and meta-analysis. Atherosclerosis. 2017;257:100-108.
5. Böhm V, Borrelli F, Capurso G. Lycopene and human health. Crit Rev Food Sci Nutr. 2021;61(1):52-86.
6. Story EN, Kopec RE, Schwartz SJ, Harris GK. An update on the health effects of tomato lycopene. Annu Rev Food Sci Technol. 2010;1:189-210.
7. Rao AV, Rao LG. Carotenoids and human health. Pharmacol Res. 2007;55(3):207-216.
8. Palozza P, Catalano A, Simone R, et al. Lycopene as a guardian of redox signaling. Acta Biochim Pol. 2012;59(1):21-25.
9. Ried K, Fakler P, Stocks NP. Effect of lycopene on blood pressure: A systematic review and meta-analysis. J Hum Hypertens. 2011;25(6):334-342.
10. Giovannucci E. Tomatoes, tomato-based products, lycopene, and cancer: Review of the epidemiologic literature. J Natl Cancer Inst. 1999;91(4):317-331.
11. Li X, Xu J, Jiang T. Lycopene and bone health: A review. Food Funct. 2017;8(5): 1837-1844.
12. Mozos I, Stoian D, Caraba A, Malainer C, Horbańczuk J, Atanasov AG. Lycopene and vascular health. Front Pharmacol. 2018;9:521.
13. Assar EA, Vidalle MC, Chopra M, Hafizi S. Lycopene acts through inhibition of IκB kinase to suppress NF-κB signaling in human prostate and breast cancer cells. Mol Nutr Food Res. 2016;60(9):2050-2060.
14. Hadley CW, Clinton SK, Schwartz SJ. The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidation. J Nutr. 2003;133(3):727-732.
15. Palozza P, Parrone N, Catalano A, Simone R. Tomato lycopene and lung cancer prevention: From experimental to human studies. Cancers. 2011;3(2):2333-2357.
16. Wang Y, Wang L, Li L, et al. The protective effect of lycopene on neurodegenerative diseases. Food Sci Nutr. 2020;8(1):16-27.
17. Riccioni G, Mancini B, di Ilio C, Bucciarelli V, Orazio N. Protective effect of lycopene in cardiovascular disease. Eur Rev Med Pharmacol Sci. 2008;12(3):183-190.
18. Böhm V, Lietz G, Olmedilla-Alonso B, Phelan D, Reboul E, Bánati D, et al. From carotenoid intake to carotenoid blood and tissue concentrations – implications for dietary intake recommendations. Nutr Rev. 2021;79(4):544-573.
19. Gajowik A, Dobrzynska MM. Lycopene – antioxidant with radioprotective and anticancer properties. A review. Rocz Panstw Zakl Hig. 2014;65(4):263-271.
20. Trejo-Solís C, Pedraza-Chaverri J, Torres-Ramos M, et al. Multiple molecular and cellular mechanisms of action of lycopene in cancer inhibition. Evid Based Complement Alternat Med. 2013;2013:705121.
21. Kim J, Lee I, Seo J, Jung J. Lycopene supplementation and oxidative stress biomarkers: A meta-analysis of randomized controlled trials. Nutrients. 2021;13(5):1602.
22. Kaur S, Sarkar S, Sharma S, Nema NK, et al. Lycopene and skin health: Current evidence and future perspective. Phytother Res. 2020;34(9):2200-2213.
23. Cheng HM, et al. The relationship between lycopene intake and stroke risk: A systematic review. Neurology. 2012;79(15):1540-1547.
24. Li X, Xu J, Jiang T, et al. Lycopene ameliorates insulin resistance: Evidence from animal studies. Mol Nutr Food Res. 2019;63(1):1800790.
25. Tang L, Lee AH, Su D, Binns CW. Association of dietary lycopene intake with the risk of ovarian cancer: A case–control study in China. Nutr Res. 2009;29(10):700-706.

Cite: Praveen Kumar Pal, Minakshi, Abhishek Singh, Pradeep Kumar, Lycopene: A Comprehensive Review of Sources, Extraction, Bioavailability, Pharmacological Activities and Future Perspectives, Int. J. Med. Pharm. Sci., 2026, 2 (4), 13-20. https://doi.org/10.5281/zenodo.19771348