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# Lycopene in Prevention and Treatment of Civilization Diseases: A Literature Review

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## ABSTRACT

Lycopene is a chemical compound that occurs in red fruits and vegetables, such as tomatoes. Lycopene has potent antioxidant and anti-inflammatory properties. Processes that influence the development of civilization diseases. The aim of the study is to explore the impact of Lycopene in the prevention and treatment of civilization diseases such as hypertension, atherosclerosis, metabolic diseases, and various cancers, in the latest research. Moreover, it will indicate directions for future research that will allow for a better understanding of the role of this compound. In conclusion, a diet rich in lycopene demonstrates potential in preventing and mitigating the severity of various civilization diseases. Therefore, the article describes a current review of research and literature in this area of knowledge. The studies presented in this article show the potential of prevention and treatment of cardiovascular, metabolic diseases, and various cancers. However, long-term studies on larger groups of subjects are needed to fully understand lycopene's potential.

**Key words:** lycopene, oxidative stress, cardiovascular diseases, cancer, civilization diseases.

## 1. INTRODUCTION

Lycopene, an organic chemical compound belonging to the carotenoid family, is a natural red dye with powerful antioxidant properties and has emerged as a significant focus in medical research. Unlike other carotenoids, lycopene is a non-provitamin A compound (Pennathur et al., 2010). It naturally occurs in red fruits and vegetables, especially tomatoes and processed tomato products, which are often used in the Mediterranean Diet. Tomato (contents of lycopene: 0.72 - 4.2 mg/100g) and tomato-based products are the source of 80% of lycopene consumption in Western countries. Lycopene can also be found in other produce such as pumpkin, carrot, watermelon, pink grapefruit, red pepper, and strawberries (Imran et al., 2020). In recent years, many studies have focused on

the potent antioxidant properties of lycopene, especially in the context of civilization diseases, which are one of the main challenges of modern medicine in an aging society. Disorders such as cardiovascular disease, obesity, type 2 diabetes, and cancer are related to oxidative stress and chronic inflammation. Lycopene, as a potent antioxidant, can play a crucial role in mitigating oxidative stress and inflammation, with preventive and therapeutic effects on cardiovascular diseases.

## 2. MATERIALS AND METHODS

The Literature review focuses on the impact of Lycopene on civilization diseases by finding and analyzing studies available in databases such as PubMed, Google Scholar, PubMed Central, and Embase. The chosen studies were published from August 2010 to January 2025, but we concentrated on the latest publications (2020-2025). In the search, we were using the following keywords: "lycopene", "oxidative stress", "antioxidant", "cardiovascular diseases", "diabetes", "cancer", "civilization diseases". Also, we used Boolean operators (OR, AND) to narrow and focus the search on the topic. Then, we analyzed and selected relevant material.

## 3. RESULTS AND DISCUSSION

### 3.1. Lycopene Properties

Lycopene ( $C_{40}H_{56}$ ) is an acyclic tetraterpenoid with a hydrocarbon structure containing 11 conjugated double bonds, giving it powerful antioxidant properties. The ability to neutralize reactive oxygen species is due to the high degree of conjugation of its double bonds. Compared to other carotenoids, it has much stronger antioxidant properties, which are crucial in protecting cells against oxidative stress. Lycopene in plant and animal organisms may occur in as trans and cis-isomers. In the human body, the isomerization process occurs in the stomach due to low pH, which is why the cis-isomer is the dominant form in human blood and tissues. Due to its lipophilic nature, lycopene is highly fat-soluble but difficult to absorb in raw food products. However, after heat treatment, especially in the presence of fat, its absorption is greatly facilitated. It is absorbed in the intestines by CD36 and B1 receptors, then transported in the blood by low-density lipoproteins (LDL). Finally, once absorbed and transported, lycopene is primarily stored in fatty tissues, liver, and adrenal glands (Imran et al., 2020; Feitelson et al., 2015; Bin-Jumah et al., 2022).

### 3.2. Lycopene and the diseases of the cardiovascular system

#### 3.2.1. Mechanisms of Lycopene's Cardiovascular Benefits

The naturally strong antioxidant properties of lycopene play an essential role in preventing cardiovascular diseases. The molecular structure of lycopene with 11 double bonds allows for the reduction of singlet oxygen and reactive oxygen species (ROS), which counteract oxidative stress. The described mechanism protects against the accumulation of excess ROS, and its consequences, such as cardiac hypertrophy, cell apoptosis, endoplasmic reticulum stress, and LDL oxidation.

By neutralizing reactive oxygen species (ROS), lycopene also has potent anti-inflammatory effects by inhibiting key inflammatory mediators such as pro-inflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8) and enzymes (COX-2, LOX). It also inhibits the proliferation of vascular smooth muscle cells and cardiac remodeling after myocardial infarction. Moreover, lycopene induces the expression of antioxidant enzymes (catalase, superoxide dismutase, and glutathione peroxidase). It increases their expression by activating the Nrf2/ARE pathway, which enhances protection against oxidative stress.

Lycopene can reduce lipids, including lowering LDL levels and modulating HDL function. New research suggests that lycopene may reduce HDL-related inflammation and modify its functionality toward an anti-atherosclerotic phenotype (Hsieh et al., 2022; Thies et al., 2017).

#### 3.2.2. Effects of Lycopene on Blood Pressure Regulation

A meta-analysis based on intervention trials suggests that daily doses of lycopene  $\geq 25$  mg effectively reduce LDL cholesterol by approximately 10%, which is a comparable effect to lower doses of statins in patients with slightly elevated cholesterol values (Ried et al., 2011).

In 2019, a study published the results of a randomized, placebo-controlled, double-blind research study that focused on the effect of Tomato Nutrient Complex (TNC) containing lycopene on blood pressure in people with hypertension. The patients received TNC with 5, 15 and 30 mg of lycopene, synthetic lycopene (15 mg) or placebo for 8 weeks. After comparing the results, it turned out that in the TNC group with 15 mg and 30 mg there was a significant reduction in systolic blood pressure. At the same time, lower doses and

synthetic lycopene alone had no significant effect. Demonstrating that TNC with lycopene (dose 15 mg and above) has a beneficial impact on systolic blood pressure (Wolak et al., 2019).

### 3.2.3. Effects of Lycopene on Atherosclerosis

A subsequent study focused on assessing the influence of lycopene on lipid metabolism. For 14 weeks researchers fed mice a diet rich in fat. The test group received daily lycopene doses (60 mg/day, human equivalent), and the control group took placebo. After the sixth week of lycopene treatment, triglycerides and cholesterol levels decreased. Moreover, lycopene significantly reduced the size of atherosclerotic plaques and the thickness of the intima-media in the aorta. These results support the use of lycopene extracts in treating atherosclerosis (Mannino et al., 2022).

### 3.2.4. Ischemic heart disease (IHD)

A study published in 2024 describes the association between ischemic heart disease and dietary intake of lycopene. A group of 443 patients with a confirmed diagnosis of ischemic heart disease and a control group of 443 people took part in the study. The amount of lycopene consumed was assessed based on a 237-item food frequency questionnaire (FFQ), after adjusting the results for other important variables such as age, gender, BMI, smoking, alcohol drinking, and physical activity. People with the highest lycopene intake had a 33% lower risk of IHD compared to those with the lowest intake (Amjadi et al., 2024).

## 3.3. Lycopene in diabetes and metabolic diseases

Lycopene, a powerful carotenoid, demonstrates significant antioxidant properties that are crucial in regulating levels of glucose in blood (Leh and Lee, 2022). Oxidative stress, which results in excessive production of ROS, damages cells, and including  $\beta$ -pancreatic cells that produce insulin (Zhu et al., 2020). Lycopene, through its antioxidant properties, reduces the production of ROS, thus supporting the redox balance in the body. Moreover, it improves insulin sensitivity, which contributes to better metabolism of glucose by cells (Kulawik et al., 2024; Jafari et al., 2025).

A study published in 2023 compared the effects of a combination of Lycopene and Metformin on Phagocytosis, Glucose regulation, and Oxidative Stress in Rats diagnosed with Type 2 Diabetes. 25 out of 30 rats had developed type 2 diabetes. For 4 weeks different groups of rats received various combinations of metformin and lycopene daily. The researchers examined phagocytosis, the level of HbA1c, reactive oxygen species (ROS), nitric oxide, and advanced glycation products. The results demonstrated that the groups with the addition of lycopene had a significantly higher phagocytosis rate and lower levels of oxidative stress markers compared to the group with metformin alone (Sianturi et al., 2023).

Moreover, there is a prospective study published in 2024 involving large sample size - 9213 adults with diabetes. Data on dietary intake of tomatoes and lycopene were obtained from two 24-h dietary recalls. Multivariate Cox proportional hazard models determined the associations between tomato/lycopene intake and mortality. The results showed lower cancer rates, and other causes in participants with higher tomato and lycopene intakes (Liu et al., 2024).

## 3.4. Impact of Lycopene in various cancers

Many researchers focus their work on the impact of lycopene on cancer processes, especially prostate cancer, but also on lung, stomach, colorectal, and breast cancer. In addition, lycopene has specific properties affecting the carcinogenic process, like anti-proliferation ability (Jiménez et al., 2024). Due to the capability to neutralize reactive oxygen species, lycopene limits the process of inflammation, DNA damage, and mutations of cells that can lead to cancer (Kapała et al., 2022). Moreover, it inhibits the proliferation and migration of cancer cells and regulates apoptosis.

Lycopene inhibits cancer cell proliferation through multiple molecular pathways by inhibiting protein complexes that control transcription of DNA, NF- $\kappa$ B activity, it also inhibits the activation of Akt pathways and mTOR, while promoting tumor suppressor proteins such as Bax and p21, and increases the phosphorylation of  $\beta$ -catenin (Feitelson et al., 2015; Puah et al., 2021).

A recent study focused on the protective effect of lycopene on preventing skin diseases. Many articles described the protective effect against skin damage by neutralizing free oxygen radicals appearing as a result of exposure to ultraviolet radiation, slowing down the skin aging process, and the possible impact on the prevention of skin cancer (Wawrzyniak et al., 2023). Table 1 summarizes the results of recent studies about the role of lycopene in various cancers.

**Table 1.** Characteristics of recent studies about the role of lycopene in various cancers.

| References              | Type of cancer    | Methods                                                                                                     | Study population                                     | Key findings                                                                                                  |
|-------------------------|-------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| (Ataseven et al., 2023) | Colorectal cancer | XTT assay, ELISA, Immunofluorescence Staining                                                               | In vitro                                             | 10 and 20 $\mu$ M lycopene doses inhibited the proliferation of HT-29 cells.                                  |
| (Sengngam et al., 2022) | Gastric cancer    | Questionnaires                                                                                              | 226 participants (80 test group, 146 control group)  | Consumption of Trans-Lycopene and $\beta$ -Cryptoxanthin reduced risk of gastric cancer.                      |
| (Dhillon et al., 2023)  | Prostate cancer   | CBMN assay                                                                                                  | 238 participants (106 test group, 132 control group) | Diet rich in lycopene minimies the DNA-damaging effects of radiotherapy.                                      |
| (Lilly et al., 2024)    | Prostate cancer   | pharmacokinetics of docetaxel, by C <sub>max</sub> and AUC <sub>inf</sub> ; CEC, VEGF-A, IGF-1R, PSA levels | 24 participants                                      | Combination of docetaxel, ADT and synthetic lycopene may support the treatment of metastatic prostate cancer. |
| (Lu et al., 2021)       | Prostate cancer   | Data from National Health and Nutrition Examination Survey                                                  | 637 participants                                     | Lycopene intake protects against a high risk of prostate cancer.                                              |
| (Mennati et al., 2022). | Breast cancer     | Synthesis of mPEG-PCL-DDAB, cytometry and gene expression analysis                                          | In vitro and In vivo                                 | mPEG-PCL-DDAB may reduce side effects because the therapeutic effect was at lower doses.                      |

### 3.4.1. Colorectal cancer

A study published in 2023 examined the effect of lycopene on the growth and apoptosis of HT-29 colorectal cancer cells. The experiment was performed on animal models and cell cultures. The samples tested apoptotic markers such as: caspase 3, BAX, activated PARP, 8-oxo-dG,  $\gamma$ -H2AX, and cytochrome c. The results showed that lycopene at doses of 10 and 20  $\mu$ M significantly inhibited the proliferation of HT-29 cells compared to the control group (Ataseven et al., 2023).

### 3.4.2. Gastric cancer

Another study focused on the association between dietary intake of Trans-Lycopene and  $\beta$ -Cryptoxanthin with gastric cancer in Vietnamese Men. The test sample was 80 men diagnosed with stomach cancer, and the control group was 146 men. The subjects completed questionnaires about diet, determining the consumption of trans-Lycopene and  $\beta$ -Cryptoxanthin, and lifestyle, and the status of Helicobacter pylori infection. The study's results indicate a positive effect of consumption of Trans-Lycopene and  $\beta$ -Cryptoxanthin, associated with a reduced risk of gastric cancer, regardless of Helicobacter pylori infection (Sengngam et al., 2022).

### 3.4.3. Prostate cancer

A larger group of studies linking lycopene with cancer concerns prostate cancer. The studies show that low levels of selenium and lycopene may increase sensitivity to radiation-induced DNA damage and suggest that a diet rich in these nutrients may play a role in minimizing the DNA-damaging effects of radiotherapy (Dhillon et al., 2023).

Considering patients with metastatic prostate cancer, there was research on the combination of lycopene with docetaxel and androgen deprivation therapy (ADT). The research group was made up of 24 people, and it showed that the highest tolerated dose of lycopene was 150 mg/day. The conclusions indicate that the combination of docetaxel, ADT and synthetic lycopene is safe and may support the treatment of metastatic prostate cancer (Lilly et al., 2024). Another study focused on checking whether a lycopene intake-

related racial disparity exists in reducing the risk of prostate cancer. Researchers analyzed data from 637 men, focusing on race/ethnicity, diet, age, living status, education level, poverty income ratio, BMI, and smoking. In conclusion, lycopene intake protects against a high risk of prostate cancer. However, this effect was only observed in a population of non-Hispanic White men. Non-Hispanic Black men had a higher risk of PCa compared to Non-Hispanic White men. In other findings: obesity had a protective effect, while living alone and being between 50 and 70 years old increase the risk of prostate cancer (Lu et al., 2021).

#### 3.4.4. Breast cancer

Many studies focus on the impact of plant-based metabolites and breast cancer therapy, including lycopene (Wali et al., 2025). Recent research has focused on a new method of treating breast cancer, combining the action of lycopene and specially designed nanoparticles with siRNA. The researchers created mPEG-PCL-DDAB molecules that transported lycopene and siRNA and blocked the pro-cancerous IGF-1R receptor. They assessed the effect on MCF-7 breast cancer cells.

The results showed that the nanoparticles had appropriate physicochemical properties, and their use significantly induced apoptosis and cell cycle arrest in the MCF-7 line. Moreover, the combination of siRNA and lycopene has demonstrated enhanced therapeutic efficacy compared to attempts to administer siRNA or lycopene alone. The use of mPEG-PCL-DDAB media may also reduce the number of side effects because the therapeutic effect was visible at lower doses (Mennati et al., 2022).

## 4. CONCLUSIONS

The synthesis of conclusions from the literature on lycopene emphasizes its role in the prevention and reduction of the risk of lifestyle diseases. In cardiovascular diseases, reducing blood pressure, slowing down the aggregation of atherosclerotic plaques, or reducing the risk of ischemic heart disease. Lycopene demonstrated a positive effect on the development of metabolic diseases by regulating glucose levels. Lycopene's properties are essential in preventing the development of cancer by neutralizing oxidative stress, reducing the intensity of inflammatory processes, and regulating the cell cycle of cancer cells. Therefore, the results of the studies presented in this article are limited. The studies differ in the daily doses of lycopene administered, the methods used, and the size of the study group. However, despite these differences, the effectiveness of a diet rich in lycopene in the prevention and treatment of lifestyle diseases is systematically confirmed in many studies. Further studies, which should be long-term research conducted on a large study group from various, diverse populations, are needed to fully understand the potential of lycopene.

#### Authors' Contributions

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All authors have read and agreed with the published version of the manuscript

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Not applicable.

#### Ethical approval

Not applicable.



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## Conflict of interest

The authors declare that there is no conflict of interest.

## Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

## REFERENCES

- Pennathur S, Maitra D, Byun J, Sliskovic I, Abdulhamid I, Saed GM, Diamond MP, Abu-Soud HM. Potent antioxidative activity of lycopene: A potential role in scavenging hypochlorous acid. *Free Radic Biol Med* 2010;49(2):205–13 doi: 10.1016/j.freeradbiomed.2010.04.003
- Imran M, Ghorat F, Ul-Haq I, Ur-Rehman H, Aslam F, Heydari M, Shariati MA, Okuskhanova E, Yessimbekov Z, Thiruvengadam M, Hashempur MH, Rebezov M. Lycopene as a natural antioxidant used to prevent human health disorders. *Antioxidants (Basel)* 2020;9(8):706. doi:10.3390/antiox9080706
- Feitelson MA, Arzumanyan A, Kulathinal RJ, Blain SW, Holcombe RF, Mahajna J, Marino M, Martinez-Chantar ML, Nawroth R, Sanchez-Garcia I, Sharma D, Saxena NK, Singh N, Vlachostergios PJ, Guo S, Honoki K, Fujii H, Georgakilas AG, Bilsland A, Amedei A, Niccolai E, Amin A, Ashraf SS, Boosani CS, Guha G, Ciriolo MR, Aquilano K, Chen S, Mohammed SI, Azmi AS, Bhakta D, Halicka D, Keith WN, Newsheer S. Sustained proliferation in cancer: Mechanisms and novel therapeutic targets. *Semin Cancer Biol* 2015;35. Suppl:S25–54. doi:10.1016/j.semcancer.2015.02.006
- Bin-Jumah MN, Nadeem MS, Gilani SJ, Mubeen B, Ullah I, Alzarea SI, Ghoneim MM, Alshehri S, Al-Abbasi FA, Kazmi I. Lycopene: A natural arsenal in the war against oxidative stress and cardiovascular diseases. *Antioxidants (Basel)* 2022;11(2):232. doi:10.3390/antiox11020232
- Hsieh M-J, Huang C-Y, Kiefer R, Lee S-D, Maurya N, Velmurugan BK. Cardiovascular disease and possible ways in which lycopene acts as an efficient cardio-protectant against different cardiovascular risk factors. *Molecules*. 2022;27(10):3235. doi:10.3390/molecules27103235
- Thies F, Mills LM, Moir S, Masson LF. Cardiovascular benefits of lycopene: fantasy or reality? *Proc Nutr Soc* 2017;76(2):122–9. doi:10.1017/S0029665116000744
- Ried K, Fakler P. Protective effect of lycopene on serum cholesterol and blood pressure: Meta-analyses of intervention trials. *Maturitas* 2011;68(4):299–310. doi:10.1016/j.maturitas.2010.11.018
- Wolak T, Sharoni Y, Levy J, Linnewiel-Hermoni K, Stepensky D, Paran E. Effect of Tomato Nutrient Complex on blood pressure: A double blind, randomized Dose–Response study. *Nutrients* 2019;11(5):950. doi:10.3390/nu11050950
- Mannino F, Pallio G, Altavilla D, Squadrito F, Vermiglio G, Bitto A, Irrera N. Atherosclerosis plaque reduction by lycopene is mediated by increased energy expenditure through AMPK and PPAR $\alpha$  in ApoE KO mice fed with a high fat diet. *Biomolecules* 2022;12(7):973 doi:10.3390/biom12070973
- Amjadi A, Alami F, Mohammadian MK, Mirshafaei SR, Azaryan F, Houshiar-Rad A, Esmaeil M, Shekari S, Abdollahi M, Khoshdooz S, Ajami M, Doaei S, Gholamalizadeh M. Association between ischemic heart disease and dietary intake of lycopene: a case-control study. *Front Nutr* 2024;10:1281539. doi:10.3389/fnut.2023.1281539
- Leh HE, Lee LK. Lycopene: A potent antioxidant for the amelioration of type II diabetes mellitus. *Molecules*. 2022;27(7):2335. doi:10.3390/molecules27072335
- Zhu R, Chen B, Bai Y, Miao T, Rui L, Zhang H, Xia B, Li Y, Gao S, Wang X, Zhang D. Lycopene in protection against obesity and diabetes: A mechanistic review. *Pharmacol Res* 2020;159(104966):104966. doi:10.1016/j.phrs.2020.104966
- Kulawik A, Cielecka-Piontek J, Czerny B, Kamiński A, Zalewski P. The relationship between lycopene and metabolic diseases. *Nutrients* 2024;16(21). doi:10.3390/nu16213
- Jafari M, Farhadi F, Baradaran Rahimi V, Rahmanian-Devin P, Askari N, Askari VR. Mechanistic insights on lycopene usage against diabetes and associated complications. *J Diabetes Metab Disord* 2025;24(1):57. doi:10.1007/s40200-025-01561-4
- Sianturi M, Susilaningih N, Nugroho H, Suci N, Kristina TN, Suryani M. Effect of lycopene and metformin combination on phagocytosis, glycemic control, and oxidative stress in rats with type 2 diabetes. *Med J Indones* 2023;32(1):1–6. doi:10.13181/mji.oa.236774
- Liu Y, Liu H, Liu J, Liu W, Yang Y, Liu Y. Associations between dietary intake of tomato and lycopene with all-cause and cancer-specific mortality in US adults with diabetes:

- Results from a cohort study. *Nutr Cancer* 2024;76(10):974–84. doi:10.1080/01635581.2024.2380521
17. Jiménez Bolaño DC, Insuasty D, Rodríguez Macías JD, Grande-Tovar CD. Potential use of tomato peel, a rich source of lycopene, for cancer treatment. *Molecules* 2024;29(13):3079. doi:10.3390/molecules29133079
18. Kapała A, Szlendak M, Motacka E. The anti-cancer activity of lycopene: A systematic review of human and animal studies. *Nutrients* 2022;14(23):5152. doi:10.3390/nu14235152
19. Puah B-P, Jalil J, Attiq A, Kamisah Y. New insights into molecular mechanism behind anti-cancer activities of lycopene. *Molecules* 2021;26(13):3888. doi:10.3390/molecules26133888
20. Wawrzyniak D, Rolle K, Barciszewski J. Lycopene – the impact of supplementation on the skin aging process. *Postepy Biochem* 2023;69(1):47–53. doi:10.18388/pb.2021\_482
21. Ataseven D, Öztürk A, Özkara M, Joha Z. Anticancer activity of lycopene in HT-29 colon cancer cell line. *Med Oncol* 2023;40(5):127. doi:10.1007/s12032-023-02001-0
22. Sengngam K, Hoc TH, Hang DV, Tran Ngoan L. Trans-Lycopene and  $\beta$ -Cryptoxanthin intake and stomach cancer in Vietnamese men: A pilot case-control study. *Asian Pac J Cancer Prev* 2022;23(3):861–5. doi:10.31557/APJCP.2022.23.3.861
23. Dhillon VS, Deo P, Fenech M. Effect of selenium and lycopene on radiation sensitivity in prostate cancer patients relative to controls. *Cancers (Basel)* 2023;15(3). doi:10.3390/cancers15030979
24. Lilly MB, Wu C, Ke Y, Chen W-P, Soloff AC, Armeson K, Yokoyama NN, Li X, Song L, Yuan Y, McLaren C, Zi X. A phase I study of docetaxel plus synthetic lycopene in metastatic prostate cancer patients. *Clin Transl Med* 2024;14(3):e1627. doi: 10.1002/ctm2.1627
25. Lu Y, Edwards A, Chen Z, Tseng T-S, Li M, Gonzalez GV, Zhang K. Insufficient lycopene intake is associated with high risk of prostate cancer: A cross-sectional study from the national health and nutrition examination survey (2003-2010). *Front Public Health* 2021;9:792572. doi:10.3389/fpubh.2021.792572
26. Wali AF, Pillai JR, Talath S, Shivappa P, Sridhar SB, El-Tanani M, Rangraze IR, Mohamed OI, Al Ani NN. Phytochemicals in breast cancer prevention and treatment: A comprehensive review. *Curr Issues Mol Biol* 2025;47(1):30. doi:10.3390/cimb47010030
27. Mennati A, Rostamizadeh K, Manjili HK, Fathi M, Danafar H. Co-delivery of siRNA and lycopene encapsulated hybrid lipid nanoparticles for dual silencing of insulin-like growth factor 1 receptor in MCF-7 breast cancer cell line. *Int J Biol Macromol* 2022;200:335–49. doi:10.1016/j.ijbiomac.2021.12.197