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Review Article

Therapeutic Potential Of Lycopene: A Phytonutrient Review

S. A. Parmar, V. Mayasa*

GITAM School of Pharmacy, GITAM Deemed To Be University, Gitam Road, Hyderabad, 502329, Telangana, India

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ABSTRACT

Lycopene is a carotenoid found in tomatoes and its derivatives. Evidence clinical studies highlights diverse therapeutic potential of lycopene. As a potent antioxidant and anti-inflammatory agent, lycopene demonstrates efficacy against various cancers, including prostate, breast, and colon cancers. Proposed mechanisms include induction cell cycle, arrest of apoptosis, and modulation of signalling pathways like IGF-1 and NF-kB. Lycopene also mitigates risk factors of diabetes by limiting blood glucose levels and increasing insulin secretion and antioxidant capacity. Additionally, it lowers LDL cholesterol, inhibits atherosclerosis progression and improves endothelial function, thereby conferring cardioprotection. Beyond these significant effects, lycopene exhibits protective roles in liver, skin, bone and nervous diseases. When applied topically, it reverses toxin-induced liver damage, prevents photoaging and dermatitis, counteracts bone loss in osteoporosis models, and shields neurons from oxidative damage. While molecular mechanisms are still being uncovered, lycopene's antioxidant, anti-inflammatory and signalling regulatory functions likely underlie its broad bioactive profile. Further research through clinical trials is warranted to elucidate optimal therapeutic dosages and preparations. Nonetheless, current evidence advocates increased dietary lycopene intake and supplementation for integrated disease prevention and adjunct therapy.

INTRODUCTION

Adverse drug reaction (ADR) is a major Lycopene, is a phytonutrient primarily present in tomatoes and its derivatives [1], cannot be produced within the human body, so it must be incorporated into one's daily dietary intake [2]. The absorbed lycopene can be found in the liver and other part of the body like skin and brain [3]. Recently, are growing fascination with the potential health advantages of lycopene. It serves as a powerful antioxidant and has garnered recognition for its positive impact on preventing and treating various diseases, as substantiated by numerous systematic reviews and meta-analyses

***Corresponding Author:** V. Mayasa
Address: , *GITAM School of Pharmacy, GITAM Road, Hyderabad, 502329, Telangana, India.*
Email : vinyasmayasa7@gmail.com

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[4]. Lycopene has shown an inhibitory effect on colorectal cancer [5], a protective role in metabolic syndrome [6], and reduced atherosclerotic plaque and improved vascular and endothelial function in various CVDs [7]. The primary dietary contributors to lycopene, making up around 80% of lycopene consumption in Western countries, are tomatoes and its derivatives. Additionally, lycopene is found in substantial quantities in foods such as watermelon, rosehips, guava, pink grapefruit, apricots, and papaya [8]. Roughly 50-65% of the overall lycopene intake is derived from natural sources,and daily contributors to lycopene intake include tomatoes, pasta dishes, ketchup, soups, and sauces made of tomato [9].

Lycopene medicinal and pharmacological effects:

Numerous global research studies have associated lycopene with a broad range of pharmacological effects and practical uses. The table below provides a concise overview of these findings, exploring various mechanisms.

Table no.1. Various mechanisms for lycopene's medicinal and pharmacological effects

Category	Mechanisms	References
Anticancer	• GF-1 levels linked to breast cancer risk. • Lycopene reduces IGF-1 levels and protects during breast cancer radiotherapy. • Lycopene extracts decrease cell viability in cancer cells like prostate cancer. • Lycopene nanoparticles reduce cell viability. • Inhibition of NNK-related receptor expression in hepatocellular carcinoma. • Lycopene impedes growth of estrogenic dependent and independent cancer cells of breast.	11,12,13,14,15,16,17,18
Antidiabetic	• Lycopene reduces diabetes-related pancreatic damage, lowers glucose, and increases insulin. • Positive effects on blood pressure and apo-I levels in type 2 diabetes. • Enhances antioxidant capacity, inhibits pro-atherogenic responses, and improves immunity.	19,20,21,22
Cardioprotective	• Lycopene inhibits cholesterol oxidation and atherosclerosis. • Reduction in cholesterol levels, improved endothelial function in hypercholesteraemic rats. • Lowers blood pressure in grade-1 hypertension. • Enhances vascular health, reduces arteriosclerosis in transplantation. • Regulation of specific pathways for cardio protection.	23,24,25,26,27,28
Antioxidative	• Lycopene is a potent antioxidant protecting DNA, proteins, and lipids. • Reduces ROS synthesis, inhibits NADPH oxidase, acts as an antioxidant, and improves liver health. • Preserves antioxidant enzyme activity, reverses hepatotoxic effects. – Enhances	29,30,31,32,33,34

	• Intestinal Barrier Function, Influences Gut Microbiota Positively. • Improves Melasma Severity, Raises Salivary Uric Acid Levels. • Mitigates Gingivitis and Reduces Lipid Peroxidation.	
Anti-Inflammatory Activity	• Lycopene addresses mitochondrial dysfunction, reduces proinflammatory cytokines in the brain. • Reduces ICAM-1 and VCAM-1 levels. • Mitigates risk of cardiovascular disease by decreasing inflammatory molecules. • Reduces oxidative stress and inflammation in obese and overweight individuals. • Lowers risk of CVD and diabetes.	35,36,37,38,39,40
Hepatoprotective	• Lycopene reduces liver injury markers and homocysteine levels. • Protects against alcohol-induced hepatic injury and stimulates cytochrome P450 2E1. • Inhibits ROS production, preserves antioxidant enzyme activity, and reverses hepatotoxicity.	41,42,43
Against Dermatologic Diseases	• Blocks upregulation of genes related to oxidative stress, photodermatoses, and photoaging by UV radiation. • Provides protection against UVB-induced erythema and downregulates proinflammatory cytokines. • Reduces proinflammatory effects on facial skin, lowering diet-related acne risk.	44,45,46,47
Neuroprotective	• Lycopene's importance in neurodegenerative diseases. • Protection against orofacial dyskinesia, improvements in biochemical and neuroinflammatory markers. • Suppression of MPTP-induced dopamine depletion, potential for Parkinson's protection.	48,49,50,51,52
Bone Protective	• Osteoporosis and lycopene's role in reducing oxidative stress and inhibiting osteoporosis. • Activation of bone-related pathways, prevention of bone loss in postmenopausal women.	53,54,55,56

Anticancer:

Inflammation is as an important factor in cancer development. Consequently, lycopene, is having potent anti-inflammatory action, is the subject of ongoing research [10]. Recently, an increasing interest in the tomato carotenoid lycopene due to its health advantages, particularly in the treatment and prevention of cancer. It is indicated that incorporating lycopene into one's diet, either through food or as a supplement, may help lower cancer risk [11]. Research involving premenopausal women has revealed a connection between elevated IGF-1 levels and a risk of cancer in the breast [12]. Interestingly, lycopene consumption has lowered blood levels of IGF-1 by promoting the production of an IGF-1 binding protein [13]. Additionally, when applied during cancer radiotherapy of the breast, lycopene has demonstrated protective properties, helping to mitigate the side effects of radiation on the skin in the treated area [14]. When human prostate cancer (PCa) cells were exposed to lycopene extracts, a notable reduction in cell viability, and an increase in apoptotic cell numbers was observed [15]. Furthermore, encapsulated in a lipid wall based material and tested on MCF-7 cells, lycopene nanoparticles exhibited a concentration and time dependent reduction in cell viability and survival [16]. In hepatocellular carcinoma, the supplementation of lycopene had several beneficial effects. It inhibited the expression of the NNK-related nicotinic acetylcholine receptor in the lungs and the activation of NF-B and CYP2E1 in the liver. Additionally, lycopene supplementation limited NNK related deaths [17]. In vitro studies conducted by Prakash et al. on cancer cells of the breast demonstrated that lycopene can impede the growth of both estrogen dependent and independent cells [18].

Antidiabetic

Various research supports the favourable impact of lycopene in the context of diabetes [19]. A diabetic rat model injected with streptozotocin, the lycopene content reduced diabetes-related pancreatic damage, lowered blood glucose and urine and levels, and increased the levels of serum insulin [20]. Farzad et al. indicated that consuming 200 grams of raw tomato per day positively impacted blood pressure and apoA-I levels associated with type 2 diabetes [21]. Neyestani et al. also identified that at physiological doses, lycopene can boost antioxidant capacity, inhibit pro-atherogenic immune responses, and enhance innate immunity in Type 2 diabetes patients, preventing long-term diabetic complications [22].

Cardioprotective

Lycopene, as a cardioprotective nutraceutical, has also been shown to prevent the oxidation of cholesterol, thereby inhibiting the initial stages of atherosclerosis [23]. In hypercholesteremic rats, the administration of lycopene resulted in significant reductions in total cholesterol, low density lipoprotein, thiobarbituric acid reactive substances, triglycerides, and very low density lipoprotein. Additionally, it led to an increase in HDL levels [24,25]. It also improved the endothelial function of cardiovascular disease patients on lycopene supplementation [26]. Engelhard et al. conducted a study showing that a brief treatment with a tomato extract can lower blood pressure in individuals with grade one hypertension who have not yet received drug therapy [27]. Lycopene has demonstrated the ability to enhance vascular health and reduce arteriosclerosis in allograft transplantation cases. This is accomplished by inhibiting the activity of kinases related to Rho and regulating the expression of NO/cGMP pathways [28].

Antioxidative

Lycopene as an antioxidant also safeguards DNA, proteins, and lipids from various oxidative damage [29]. In an animal study, lycopene had several positive effects. It significantly reduced the synthesis of ROS in SK-Hep-1 cells by inhibiting NADPH oxidase. Additionally, lycopene was effective in countering liver toxicity via it's antioxidative action, regulating total catalase and glutathione levels, limiting glutathione disulfide, preventing oxidative damage through the reduction of protein carbonylation, and upregulating MMP-2 down-regulation [30]. Another study suggests that lycopene supplementation increased intestinal barrier activity and positively influences the gut microbiota in weaned piglets by modulating antioxidant signaling pathways in the intestinal [31]. Melasma affects approximately 40% of individuals in Southeast Asia and is often induced by oxidative stress from ultraviolet radiation, which activates the melanogenesis pathway. To address this, supplementation with a lycopene-rich tomato extract increased serum superoxide dismutase (SOD) levels and improved melasma outcomes, making it a promising adjuvant therapy [32]. Periodontitis emergence has mainly been due to elevated oxidative stress. A study evaluated that oral supplementation with lycopene and green tea extract was linked to increased salivary uric acid levels and plays a crucial role in gingivitis management [33]. Oral lichen planus, an autoimmune condition, is typically treated with topical steroids. The side effects of systemic corticosteroids in cases of resistant oral lichen planus make it necessary to consider alternative treatment options. According to study findings, lycopene is a safe and effective therapeutic option for managing resistant oral lichen planus. It can reduce 8-isoprostane, a biomarker of lipid peroxidation [34].

Anti-Inflammatory Activity

Lycopene has shown effectiveness in addressing mitochondrial dysfunction triggered by A1-42 in conjunction with elevated proinflammatory cytokines such as IL-1, TGF, and TNF-alpha, as well as the activation of caspase-3 and NF-B in the brains of rats [35]. Additionally, lycopene reduces the levels of ICAM significantly and vascular cell adhesion molecule 1 [36]. Colmán-Martínez et al., conducted a study on the impact of carotenoids obtained from tomato juice (TJ) on inflammatory biomarkers was assessed through a 4-week dose-response nutritional trial involving a population at a high risk of CVD. The findings suggest that trans-lycopene from tomato juice can potentially mitigate the risk of CVDs by decreasing the levels of key inflammatory molecules liked with atherosclerosis [37]. Moreover, consumption of tomato and its products has been linked to reduced oxidative stress and exerts a beneficial effect on endothelial function through antioxidant and anti-inflammatory action [38]. It also reduces inflammation in obese and overweight females, reducing the risk of CVD and diabetes [39]. Burton-Freeman et al. included tomato products in a meal to reduce the oxidative stress and inflammatory response induced by post-meal increases in blood lipids (postprandial lipemia), and the findings proposed that tomatoes may play a significant protective role in lowering the risk of cardiovascular disease [40].

Hepatoprotective:

Yefsah-Idres et al. expressed that lycopene administration is having a beneficial action on liver health by reducing levels of alanine aminotransferase, aspartate aminotransferase, and serum homocysteine, indicating an amelioration of liver injury [41]. Furthermore, research has indicated that tomato powder can serve as a protective substance against liver injury induced via alcohol by stimulating cytochrome P450 type 2E1, an enzyme metabolising alcohol and other substances in the liver [42]. It was also observed with a combined with proanthocyanidins in preventing mercuric chloride induced liver damage in animal studies. The results expressed that the combination inhibited the production of ROS, preserved the function of antioxidant enzymes, and reversed the hepatotoxic effects caused by mercuric chloride in the liver of rats [43].

Against Dermatologic Diseases

A study investigated lycopene-rich tomato nutrient complex and lutein to provide protection against both UVA/B and UVA1 radiation. The findings revealed that TNC effectively blocked the upregulation of intercellular adhesion molecule 1, heme-oxygenase 1, and MMP-1 mRNA. These genes are known indicators of oxidative stress, photodermatoses, and photoaging [44]. A carotenoid-containing supplement, well-tolerated by the participants, provided significant protection against the formation of erythema (skin redness) induced by UVB radiation. It also reduced proinflammatory cytokines in healthy volunteers [45]. A study assessed the effects of new lycopene enriched ice cream on systemic antioxidant properties and its impact on the physical characteristics of facial skin. The results indicated that this ice cream could reduce the proinflammatory effects on facial skin, consequently lowering the risk of diet-related acne development in young consumers [46]. Moreover, a lycopene-based topical emulgel was developed and showed a potent antioxidant potential, preventing acne oxidative stress-related skin disorders and reduced the ageing process [47]

Neuroprotective

Neurodegenerative diseases, are a significant health concern in developed societies, responsible for about 60% of cases. Such conditions are primarily due to factors like ageing populations and unhealthy lifestyles, environmental factors, heightened ROS activity, inflammation, injuries and genetics [48]. Neuron cell membranes contain high polyunsaturated fatty acids, making them vulnerable to oxidation. Furthermore, the central nervous system has limited regenerative capacity, impeding its recovery and function after damage caused by reactive oxygen species (ROS) [49]. With its antioxidant properties, lycopene plays an important role. Its lipophilic nature of lycopene allows it to easily cross the blood-brain barrier and protect against oxidative stress-induced damage, making it particularly important for neural health [50]. In a different study, lycopene administration had a significant positive impact on rats with haloperidol-induced orofacial dyskinesia. It improved biochemical, behavioural, neuroinflammatory, and neurochemical markers associated with this condition [51]. In the case of Parkinson's disease, a study demonstrated a 7-day treatment with lycopene effectively prevented the depletion of striatal dopamine induced by MPTP in mice. These findings suggest that lycopene supplementation may protect dopaminergic neurons against stimuli that induce Parkinson's disease [52].

Bone Protective

Osteoporosis is a prevalent metabolic condition that affects the bone tissue. It involves a shift toward increased bone resorption compared to bone formation, leading to decreased bone mass and strength. This condition elevates the risk of fractures in affected individuals [53]. Rivas et al. suggested that a diet rich in lycopene may play a role in reducing oxidative stress, thereby mitigating the detrimental impact of ROS on bone cells and potentially inhibiting the development of osteoporosis [54]. A study found that lycopene activates specific cellular pathways, including WNT/β-catenin and ERK1/2, which upregulate essential bone markers collectively, helping to prevent bone loss in postmenopausal women [55] and reducing the risk of bone resorption by oxidation prevention [56].

CONCLUSION:

This review highlights the diverse therapeutic potential of lycopene, a phytonutrient found abundantly in tomatoes and tomato-based products. The research synthesized here demonstrates lycopene's efficacy as a potent antioxidant and anti-inflammatory agent, making it a promising neutraceutical for preventing and treating various diseases. The anticancer properties of lycopene are well-documented, with studies indicating its effectiveness against cancers of the prostate, breast, liver, and colon. Mechanisms like cell cycle arrest, apoptosis induction, and signalling pathway modulation underlie lycopene's antitumor effects. Additionally, lycopene reduces risk factors for diabetes by lowering blood glucose, increasing insulin secretion, and boosting antioxidant status.

It also mitigates cardiovascular disease progression by lowering LDL cholesterol, inhibiting atherosclerosis, and improving endothelial function. Beyond these significant therapeutic applications, lycopene demonstrates protective effects on the liver, skin, bones and nervous system. When applied topically, it reverses liver damage induced by toxins, provides defence against photoaging and dermatitis, prevents bone loss in osteoporosis, and shields the brain from oxidative damage. While the molecular mechanisms are not yet fully elucidated, lycopene's antioxidant, anti-inflammatory and signalling regulatory functions likely mediate its broad spectrum of bioactivities. Further research through rigorous clinical trials is needed to establish optimal therapeutic dosages and standardize preparations. Nonetheless, current evidence strongly advocates increased dietary lycopene intake and supplementation for disease prevention and integrated adjunct therapy. Incorporating tomato products into daily nutrition is a prudent strategy to harness the health benefits of this multifaceted phytonutrient.

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CONFLICT OF INTEREST:

The authors declared that there is no conflict of interest

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