



## Lycopene and Cardiovascular Disease: An Overview

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### Abstract

Cardiovascular Disease (CVD) is a major cause of mortality and disability in Western countries. Prevention is essential to reduce the incidence of cardiovascular diseases and also to reduce the costs both of citizen and health system. In general, cardiovascular diseases are closely associated not only with problems related to oxidative stress, but also to inflammatory processes and vascular dysfunction. Lycopene is a bioactive component mainly found in tomatoes, redfruits and vegetables, from chemical point of view. It is a hydrocarbon belonging to tetraterpene carotenoids and presents eleven conjugated double bonds that are directly responsible for the antioxidant and anti-radical properties of lycopene, especially for reactive oxygen species and nitric oxide. This compound has the highest antioxidant power among all carotenoids and its properties are correlated with many beneficial effects, including its potential cardioprotective role. Many epidemiological studies have shown an association between consumption of tomato or lycopene products and a lower risk of CVD. In particular, several studies suggest a role of lycopene in the primary prevention of cardiovascular diseases, and for this reason, this review focuses on the available evidence regarding the effects of lycopene on the cardiovascular system and on the multiple benefits from its potential use as a drug and/or nutraceutical.

**Keywords:** Lycopene; Carotenoids; Cardiovascular disease; Antioxidant

### Introduction

Carotenoids are a group of C-40 isoprenoid-based molecules with > 600 representatives in nature. Lycopene is one of the most representative carotenoids naturally found in plants, bacteria, fungi, and algae [1]. This class of phytochemicals has recently attracted much attention due to potential health beneficial effects associated with carotenoid intake and food rich in carotenoids. Lycopene is a fat-soluble pigment synthesized by plants and microorganisms and is responsible for the red colour to vegetables and fruits. The main natural source can be considered tomato and tomato products. It is considered as one of the most effective single oxygen species in carotenoids and its inactivation capacity is twice that of beta carotene and 100 times that of vitamin E [2]. As reported in various studies, lycopene is known as the most powerful antioxidant among major carotenoids detected in human tissues or blood [3] and it may have an inhibitory effect on cholesterol synthesis which may enhance the Light Density Lipoprotein LDL degradation [4,5].

In general, carotenoids play a very important role as scavengers of free radicals in humans and plants [6], in fact they confer antioxidant protection to the plant and are responsible for the change of color during maturation, and for the improvement of the attraction, consumption and dissemination of seeds by herbivores [7,8]. Cardiovascular Disease (CVD) is a major cause of mortality and disability in Western countries. In particular, atherosclerosis-related cardiovascular diseases are the leading cause of mortality world wide, and the main cause of death under 75 years old in Western countries, with a huge social and economic impact [9,10]. From this point of view, it is important to set up new strategies to fight this kind of disorders and the use of bioactive compounds or nutraceuticals could be useful for this scope. In fact, several clinical and epidemiological studies have confirmed that diets rich in lycopene are associated with the prevention or reduction of the risk of CVD [11], reduced risk of developing prostate lung and ovarian cancers and with a lower incidence of chronic degenerative diseases [12-14]. It is interesting to note that some more recent studies indicated that lycopene intake present in tomato fruit is more effective in preventing certain types of cancer than the administration of purified lycopene by capsules [15].

### Chemistry of Lycopene

The pigment lycopene belongs to the subgroup of non-oxygenated carotenoids, being characterized by 11 conjugated double bonds. Its molecular formula is C<sub>40</sub>H<sub>56</sub> and 536.88 is its

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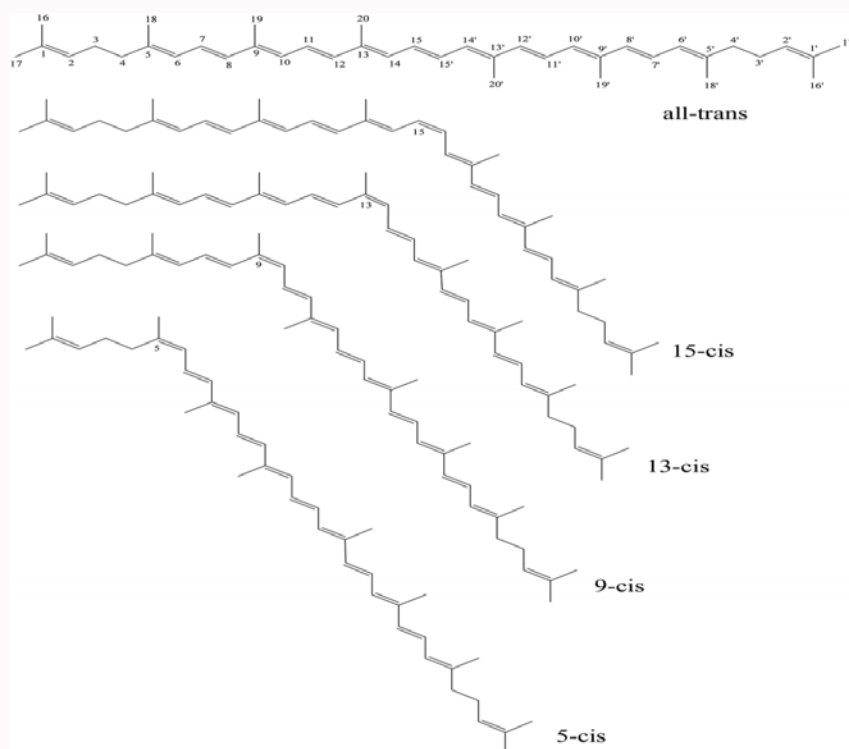
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**Figure 1:** Chemical structure of all-*trans* lycopene and the main *cis* forms.

molecular weight. Lycopene is a symmetrical molecule formed from eight C5 isoprenoid units joined head-to-tail, except at the center, where there is a tail-to-tail link that reverses the order (Figure 1). Generally the carotenoids in dietary sources are found in the linear, all-*trans* conformation, while human tissues contain mainly *cis*-isomers. Several research groups have suggested that *cis*-isomers of lycopene are better absorbed than the all-*trans* form because of the shorter length of the *cis*-isomer, the greater solubility of *cis*-isomers in mixed micelles, and/or as a result of the lower tendency of *cis*-isomers to aggregate. Normally, in processed foods it is mainly in the form of the isomers.

### Cardiovascular Protection

Many research articles and epidemiological studies have closely linked the use of lycopene from food or as a food supplement and the reduced risk of developing CVD. In a review article, Costa-Rodrigues, Pinho and Monteiro (2018) [16] considered the various biological activities of lycopene and in particular assessed the cardioprotective properties of this compound. Recently, a systematic review and meta-analysis was conducted, concerned with the effects of lycopene and cardiovascular function [17]. In particular, in this review only interventional studies were studied with human subjects with food exposure to tomato-based products or lycopene supplements, for a total of twenty-two publications. Overall, the analyzed data show that lycopene promotes both a decrease in LDL cholesterol levels in plasma and an increase in endothelial function. Regarding the LDL reduction effect, it is important to stress that, once again, only foods containing lycopene, but not lycopene-based supplements, have been able to promote it. In a recent meta-analysis study published in 2017 [18], the relationship between lycopene intake, plasma levels and cardiovascular disease was evaluated. Analysis of the data showed that lycopene was associated with a 17%

reduction in the risk of cardiovascular disease, when the results of the higher intake were compared to the low intake. Several mechanisms have been proposed to explain the cardiovascular protective effects of lycopene, including the reduction of cholesterol levels and inflammatory response, the reduction of oxidation of biomolecules, the improvement of intercellular communication and the stimulation of apoptosis and finally, the antiangiogenic effects. Tomatoes are considered the primary source of lycopene, one of the most powerful antioxidants known, and are therefore able to reduce oxidative stress induced by reactive oxygen species, inflammation and platelet aggregation. Thanks to the high content in lycopene, tomatoes are able to reduce lipid peroxidation and low density lipoproteins [19]. It is important to remember that all these factors play a fundamental role in the development of atherosclerosis and CVD. In a study carried out by Jacques and coworkers (2013) [20] an inverse association between lycopene intake and CVD risk has been highlighted, while, in the same study, lycopene intake was unrelated to stroke incidence. It's important to note that in order to overcome potential classification errors of lycopene intakes, that would lead to unreliable results, the authors of this work used repeated measures of intake obtained over 10 years to characterize the relationship between lycopene intake and the incidence of CVD, Coronary Heart Disease (CHD) and stroke.

### Concluding Remarks

In recent years there has been an increase in the demand for natural health products for which the search for new remedies for the prevention and treatment of chronic diseases that are disabling and of great impact and diffusion has become a central topic for researchers working in food and health sector. From this point of view, the scientific data of recent years that have attributed to lycopene and food products rich in lycopene, significant health properties, suggest an use of this molecule in the prevention and treatment of diseases

affecting the cardiovascular system. Carotenoids have been reported to prevent or reduce the risk of CVD. In fact, in several clinical and epidemiological studies have confirmed that diets rich in lycopene are associated with reduced risk of developing prostate lung and ovarycancers and a lower incidence of chronic degenerative diseases and cardiovascular diseases. It is interesting to note that some more recent studies indicated that lycopene intake present in tomato fruitis more effective in preventing certain types of cancer than the administration of purified lycopene by capsules.

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