The Antidiabetic and Antioxidant Effects of Carotenoids: A Review

Miaad Sayahi1 and Saeed Shirali2,3*

1Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2Hyperlipidemia Research Center, Department of Laboratory Sciences, Faculty of Paramedicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3Research Center of Thalassemia and Hemoglobinopathy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; sayahi.m2014@gmail.com

Abstract

Carotenoids are a big group of phytochemicals that have a wide variety of protective and medical properties. They are widespread in plants and photosynthetic bacteria and have many medical functions. Here in this article, we studied antidiabetic and antioxidant effects of four kinds of carotenoids (lutein, lycopene, beta-carotene and astaxanthin) besides briefly defining them and also mentioned some of their plant sources. So, we can say, the aim of this study was to show some of the ways they can lower blood glucose and prevent the oxidant damages. Many articles, including originals and reviews were scanned in this way, but only a few had a suitable data. All of our references were articles has been collected electronically from valid journals and databases including PubMed, Science Direct, Elsevier, Springer and Google scholar. Beta-carotene is the most widely carotenoid in food prevent cancer and triggers the release of insulin and like lutein its antioxidant is useful for the prevention of macular degeneration. Lutein has also anticancer effects and reduces the ROS levels in the retina with diabetes. Lycopene helps to protect diabetes patients with cardiovascular disease. Astaxanthin has significant hypoglycemic effects. Both of lycopene and astaxanthin have powerful antioxidant activity. We suggest that each of these phytochemicals produces a kind of protect against diabetes and oxidative damages and also have other medical functions like anticancer, anti-inflammatory but further and deeper investigations are required in this field.

Keywords: Antidiabetic, Antioxidant, Astaxanthin, β-Carotene, Lutein, Lycopene, Phytochemical

1. Introduction

Reports from the World Health Organization (WHO) indicate that diabetes mellitus is one of the major killers of our time1. A long-term increase in glucose is one of the most important causes of diabetes secondary disorders such as angiopathy, neuropathy, retinopathy, deficiency in the antioxidant defense system, and lipid profile disorders2. Hyperglycemia alone does not cause diabetic complications. It is rather the detrimental effect of glucose toxicity due to chronic hyperglycemia, which is mediated and complicated through oxidative stress1. The single unifying mechanism of oxidative stress due to persistent hyperglycemia, which leads to an overt generation of ROS (Reactive Oxygen Species) in mitochondria, results in a variety of harmful oxidative products. Normalizing levels of mitochondrial, ROS have been shown to prevent the formation of these products3-4. Plants have been used for medicinal purposes across history and cultures and even across species. A majority of the world still relies heavily on herbal remedies for their primary health care. With the increasing movement of people across countries, there is an accompanying movement of their respective traditional medicines5. Phytochemicals are non-nutritive plant chemicals that have protective properties and have secondary metabolites in plants which provide much of the color and taste in fresh or processed fruits and vegetables. The plant produces these chemicals to protect itself, but recent research demonstrates that many phytochemicals can protect human against diseases6.
Carotenoids are widespread phytochemicals in plants and in photosynthetic bacteria, where they serve two essential functions: as accessory pigments in photosynthesis and in photoprotection. These two functions are a result of the conjugated polyene structure of carotenoids, which allows the molecule to absorb light and to quench, or inactivate, singlet oxygen and free radicals. Human, mostly consume a variety of different carotenoids, including those occurring naturally in foods (primarily fruits and vegetables) and those added as food colorants. Provitamin A carotenoids can be converted enzymatically in the intestinal mucosa to yield retinal and ultimately retinol; retinol (vitamin A) is required for vision, maintenance of differentiated epithelia, mucus secretion, and reproduction. Not all dietary carotenoids are metabolized in the intestinal mucosa following ingestion. Numerous epidemiologic studies have shown that individuals who consume a relatively large quantity of carotenoid-rich fruits and vegetables have a decreased risk of cancer at several tumor sites, as reviewed elsewhere. The mechanism by which carotenoids protect biological systems against O₂⁻ mediated damage appears to depend largely on physical quenching. Most carotenoids contain an extended system of conjugated double bonds, which is responsible for their antioxidant activity. Carotenoids have also been shown to be capable of inhibiting free radical reactions. The use of phytochemicals in the treatment of diseases is on the rise. Also, determination of the contents of phytochemicals and plant extracts is important. Here, in this article we chose four carotenoids that have the most relationship with diabetes and antioxidant activities, including β-carotene, lycopene, lutein and astaxanthin and beside pointing out their bioactivities and therapeutic claims, tried to emphasize their antidiabetic and antioxidant effects to show some of the ways they can lower blood glucose and prevent the antioxidant damages and also mentioned their herbal sources.

2. β-Carotene

Beta-carotene (BC) is a member of naturally occurring compounds called carotenoids which are a group of phytochemicals. β-Carotene is an antioxidant and is one of the forms of carotene that colored red-orange pigment and widely found in nature, abundant in plants and fruits, especially in orange fruits such as cantaloupe, mangoes, pumpkin, and papayas, and orange root vegetables such as carrots and sweet potatoes. The color of β-carotene is masked by chlorophyll in green leafy vegetables such as spinach, kale, and broccoli. It prevents a different type of cancers, by protecting cells in the body against oxidation damage by free radicals, by scooping them up and also by generating other antioxidants. What's more, it can also be converted to vitamin A as needed.
instance, β-apo-8’-carotenal and 6’-methyl-β-apo-6’-carotene-6’-one (citranaxanthin)14.

3. Lycopene

Lycopene is a lipophilic compound with a 40-carbon linear structure. Lycopene belongs to the family of fat-soluble plant pigments called carotenoids17. It is one of the major carotenoids found in tomatoes and tomato products. Unlike β-carotene it lacks a β-ionone ring, so it cannot be converted chemically to vitamin A. Lycopene is a bright red pigment that is naturally found in the human liver, serum (blood), adrenal glands, lungs, prostate, colon, and skin at higher levels than other similar pigments. Food processing may improve lycopene bioavailability and absorbance in two ways: (a) breaking down cell walls, which weakens the bonding forces between lycopene and the tissue matrix, thus making lycopene more accessible; and (b) enhancing the isomerization. After absorption of dietary fat, lycopene is transported via intestinal lymphatic to the liver by chylomicrons. Lycopene leaves the liver in a VLDL (very low-density lipoprotein) particle, the precursor of LDL. Under fasting conditions, lycopene circulates as part of LDL (low density lipoprotein). That is why usually a positive correlation exists between serum levels of lycopene and cholesterol17. A red pigment, lycopene is commonly found in fruits and vegetables of that hue. It may be the most abundant nutrient of the carotenoid family related to prostate health18. Over the last decade, there has been increased recognition that lycopene plays an important role in preventing the development of CHD (Coronary Heart Disease) and retarding the progression of atherosclerosis. In mice, lycopene has shown protection against the development of breast tumors19.

![Chemical structure of lycopene](image)

**Figure 2.** Chemical structure of lycopene (MW: 536.88; Formula: C₄₀H₅₆)13.

Diabetic patients may suffer from complications as vascular disease, diabetic neuropathies or infections. Lycopene helps to protect diabetes patients against cardiovascular disease and may improve the immune response13. Tomato paste, a tremendous source of this nutrient, has demonstrated some protection against the development of cardiovascular disease80. However, the consumption of lycopene seems not to reduce the risk of diabetes mellitus type 213. Though not a pro-vitamin A, lycopene has attracted attention as a potent natural antioxidant. The antioxidant activity of lycopene is almost twice as high as that of β-carotene and has the greatest synergism with vitamin E17. This antioxidant activity of 13-carotene, which would be shared by other carotenoids as well because it depends on the formation of a resonance-stabilized carbon-centered radical, may contribute to the protection of membranes from lipid peroxidation. Autoxidation of 13-carotene leads to the formation of epoxides located at the 13-ionone ring and to ketones (13-apocarotenones) and aldehydes (13-apo-carotenals) of different chain lengths. At low concentrations and at partial pressures of oxygen, such as those found in most tissues under physiologic conditions, 13-carotene was found to inhibit the oxidation of model compounds (tetralin and methyl linoleate) by peroxyl radicals11. Lycopene also shows benefit for the blood vessels around the heart, demonstrating protection to the blood vessels in the neck, better than vitamins A, E or CoQ10. This isn't much of a surprise since lycopene is regarded as a powerful antioxidant. Higher levels of this antioxidant have also shown protection against heart attack21. It is possible that anything red has some degree of lycopene, sure, but we should focus on incorporating tomato products regularly. Aside from the popular tomato, other sources of lycopene include red grapefruit, watermelon and apricots17.

4. Lutein

Lutein is an antioxidant carotenoid a pigmented nutrient that is responsible for the yellow colors of fruits and vegetables and is present in the highest quantities in dark, leafy green vegetables. You’re born with a certain amount of lutein in your eye, but your body doesn’t reproduce it. The macula is the region of the retina responsible for central vision. Lutein helps protect against this damage by filtering blue light before it can damage the macula22. It is related to beta-carotene and vitamin A. Lutein is one of two major carotenoids found as a color pigment in the human eye (macula and retina). Many people think of lutein as “the eye vitamin.” They use it to prevent eye
diseases, including Age-related Macular Degeneration (AMD), cataracts, and retinitis pigmentosa. Some people also use it for preventing colon cancer, breast cancer, type 2 diabetes, and heart disease.

5. Astaxanthin

Astaxanthin (3',30-dihydroxy-b, b-carotene-4, 40-dione), a keto-carotenoid pigment, with no pro-vitamin A activity, is a carotenoid that has many highly potent pharmacological effects such as potent antioxidative activity, immunomodulating actions, anticancer activity, and anti-inflammation action. Astaxanthin's pharmacological effects in animal models are extensive, ranging from protection against Helicobacter pylori-induced gastric inflammation and the protection from hepatotoxicity by carbon tetrachloride to increase immune function.

In a study, results suggest that the astaxanthin from shrimp waste produces a significant hypoglycemic effect after oral administration in alloxan-induced diabetic mice. As presented in the “Result” the hypoglycemic effect of 10 mg/kg dose was to that of metformin. Postprandial hyperglycemia was significantly suppressed by oral administration of astaxanthin, which significantly lowered the postprandial AUC. Therefore, it can be said that astaxanthin is a useful natural agent in treating diabetes.

Astaxanthin is reported to be a potent antioxidant and inhibits low-density lipoprotein oxidation induced by azo-compound. Astaxanthin has a high antioxidant activity due to the presence of the hydroxyl and keto endings on each ionone ring. It has been reported in the literature that the antioxidant activity of astaxanthin is approximately 10 times higher than other carotenoids such as zeaxanthin, lutein, canthxanthin, beta-carotene, and about 100–500 times than that of alfa-tocopherol. Some findings suggest that astaxanthin may diminish the oxidative stress caused by hyperglycemia in the pancreatic "cells. 
Astaxanthin is a powerful biological antioxidant that occurs naturally in a wide range of organisms, including salmon, trout, shrimps, lobsters, yeast, algae, fish, and birds.

6. Conclusion

As mentioned carotenoids are a big group of phytochemicals that have a wide variety of protective and medical properties. In this article, we studied antidiabetic and antioxidant effects of carotenoids including lutein, lycopene, beta-carotene, and astaxanthin. We suggest that each of these four phytochemicals has properties to protect against diabetes and oxidative damages and also have other medical functions like anticancer and anti-inflammatory activities but further and deeper investigations are required in this field.

7. References