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Astaxanthin in Disease Prevention and Treatment

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Abstract. Astaxanthin is a carotenoid with strong antioxidant activity. The function of astaxanthin has been associated with a number of health-promoting benefits. This paper discusses the beneficial effects of astaxanthinin the prevention and treatment of human diseases such as cardiovascular diseases, cancer, diabetes and neurodegenerative diseases.

Introduction

Astaxanthin is a ketocarotenoid with strong antioxidant activity, which belongs to the family of xanthophylls [1, 2]. It occurs naturally in a wide variety of organisms such as microalgae, yeast, salmon, trout, shrimp and crayfish. The function of astaxanthin has been associated with a number of health-promoting benefits. This paper reviews the beneficial effects of astaxanthin in the prevention and treatment of human diseases such as cardiovascular diseases, cancer, diabetes, mellitus antidiabetic, and neurodegenerative diseases.

Astaxanthin and Cardiovascular Disease

Astaxanthin has been regarded as a potential treatment for cardiovascular diseases [3]. Both *in vitro* and *in vivo* studies shows that astaxanthin can reduce the oxidation of low density lipoprotein (LDL) [4]. Astaxanthin alsodose-dependently reduces the levels of triglyceride and increases serum high density lipoprotein (HDL)-cholesterol andadiponectin, which is a protein hormone modulating a number of metabolic processes including glucose regulation and fatty acid oxidation[5]. The disruption of mitochondrial membrane potential (MMP) is associated with apoptosisin cardiac cells. Astaxanthin elevates the MMP in heart dose-dependently, attenuating the release of cytochrome c from mitochondria and thereby inhibiting apoptosis and contractile failure and consequently improving cardiac function[6].Oxidative stress and inflammation are strongly linked to the development of cardiovascular diseases. Study has shown thatastaxanthin inhibits the inflammation and oxidative stress in human umbilical vein endothelial cells[7]. In stroke-prone hypertensive rats, it has been found that astaxanthin suppresses blood pressureand inhibits thrombosis in cerebral vessels [8]. Therefore, astaxanthin may contribute to the prevention of atherosclerosisand cardiovascular disease by regulating the levels of LDL and HDLand by reducing blood pressure,inflammation and oxidative stress.

Astaxanthin and Cancer

Astaxanthin has been shown to have anti-cancer effects [9].In gastric cancer cell

model, astaxanthin inhibited cell proliferation through extracellular regulated protein kinases (ERK)-mediated cell cycle interruption. In hepatoma cells, astaxanthin not only disturbed the cell cycle, but also induced cell apoptosis [10]. In lung cancer cells, astaxanthin increased the apoptosis induced by chemotherapeutic agent mitomycin C by suppressing the activation of Akt and Rad51[11]. In a hamster oral cancer model, astaxanthin modulated the Nuclear factor-κB (NF-κB) and Wnt/β-catenin pathways, causing the apoptosis in the buccal pouch tissue[12]. It was also demonstratedin hamster oral cancer model thatastaxanthin interrupted cell proliferationvia STAT-3-mediateddecrease of cyclin D1 levels and increase of p21 expression while impeding the cell invasion by suppressing the expression of matrix metalloproteinases-2 (MMP-2) [13]. Similarly, astaxanthin alleviated the invasion of colon cancer induced by dimethyl hydrazine in Wistar rats by reducing the expression of MMP-2[14]. Overall, astaxanthin inhibits tumorgenesis by interruption of cell proliferation,promotion of apoptosis and decrease of cell invasion.

Astaxanthin and Diabetes

The major pathological feature of diabetes mellitus is impaired insulin secretion/sensitivity and the disease is frequently diagnosed by hyperglycemia, lipid abnormalities and vascular complications. In diabetic db/db mice, astaxanthin can attenuate blood glucose levels [15]. The immune dysfunction and oxidative stress are common in diabetic patients. indiabetic rats, the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and the levels of glutathione in liver are significantly decreased, which can be reversed by astaxanthin treatment [16]. In diabetic lymphocytes, astaxanthin can alleviatelymphocyte dysfunctions by significantly decreasing the production of $NO^{\bullet}$ and $O_2^{\bullet-}$ and reducing the cytosolic Ca^{2+}[17].In diabetes, major damage occurs in tissues such as kidney, astaxanthin can protect cell damages in thediabetic kidney[18]. In the kidneys of astaxanthin fed diabetic mice, cells positive for 8-hydroxydeoxyguanosine(8-OHdG), an index of oxidative stress, were significantly decreased, thus leading to the prevention of diabetic nephropathy[15]. One of the pathogenic factors of cardiovascular complications in diabetes is glycemic fluctuation. In endothelial cells, astaxanthin suppressed glucose fluctuation-induced signals such as the activation of c-Jun N-terminal kinase and p38mitogen-activated protein kinase, so astaxanthin may have protective effects against glucose fluctuation-induced endothelial dysfunction[19].

Astaxanthin and Neurodegenerative Diseases

Oxidative stress has been implicated in the pathogenesis of neurodegenerative disease. By reducingoxidative stress, astaxanthin has been shown to protect neuronal cells from reactive oxygen species-mediate toxicity [20], and decrease ischemia/reperfusion-induced hippocampal pyramidal neuron loss and learning and memory deficits [21]. Astaxanthin has also been shown to inhibit aluminum-induced activation of glial cells and generation of reactive oxygen species, consequently improving the spatial memory and locomotor activity in aluminum-treated animals [22]. In neuronal cell model and primary hippocampal neurons, astaxanthin can reduce the toxicity of β-amyloid (Aβ), which plays an important role in the pathogenesis of Alzheimer’s disease (AD), by alleviating the oxidative stress induced byAβ [23]. 1-methyl-4-phenylpyridinium ion (MPP^+) is a neurotoxinis that damages dopamine absorption and stimulates dopaminergic neuronal death, leading to Parkinson's disease-like syndrome. Astaxanthin has been shown to protect against

MPP^+-induced oxidative stress and cell damages in both cell and animal models[24, 25]. Thus, astaxanthin may be a potential therapeutic agent in neurodegenerative diseases [26].

Astaxanthin and Other Disease

It has also been demonstrated that astaxanthin may be beneficial to a number of other disease conditions such as nonalcoholic fatty liver disease, lung fibrosis andacute kidney injury.The dysregulation of fibrogenesisin hepatic stellate cells isa common feature of non-alcoholic fatty liver. Inhuman hepatic stellate cell line LX-2 cells and primary mouse hepatic stellate cells, astaxanthin inhibited fibrogenesis through attenuating cell signals mediated by fibrogenic cytokine transforming growth factor β1(TGFβ1) [27]. In high-fat-fed mice, astaxanthin administrationreduced hepatic lipid accumulations and attenuated hepatic autophagy possibly via activatingperoxisome proliferator-activated receptor alpha and inhibiting peroxisome proliferator-activated receptor gamma [28].Astaxanthin also inhibited apoptosis induced by reactive oxygen species in animal models of lung fibrosis and acute kidney injury, alleviating these pathologic conditions[29, 30].

Summary

In summary, astaxanthin has beneficial effects in a number of humandiseases. And astaxanthin may have therapeutic potential for prevention andtreatment of these diseases.

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