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# The Role of Carotenoids in Prevention and Treatment of Multiple Diseases

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**ABSTRACT**:Carotenoids are biologically active compound with antioxidant properties, playing important role different diseases and human health. They exhibit significant properties such as antioxidant, anti-viral, anti-bacterial, anti-cancer property in human body. Consumption of specific carotenoids lessen the probably of multiple diseases and infections like as cancer, tuberculosis, ophthalmic infections, and neurodegenerative diseases. Carotenoids such as lutein, beta-carotene, zeaxanthin, lycopene are involved in different metabolic functions in our body. Lycopene is an important carotenoid which exhibit cancer preventive functions due to its antioxidant properties and it is also involved in reducing the blood pressure in hypertensive persons. In this review, we describe the sources, bioavailability, and the preventive and therapeutic role of carotenoids in multiple diseases.
**KEYWORDS:**Antioxidant, Bioavailability, Cancer, Carotenoids, Diseases, Prevention.

## I. INTRODUCTION

Carotenoids are beneficial in the prevention of different diseases because of their antioxidant properties. Carotenoids are coloured compounds plentifully present in vegetables and fruits and microorganism. α- carotene, zeaxanthin, lycopene, β-carotene, lutein and β-cryptoxanthin are found in human [1]. Carotenoids play significant role in boosting the immune system, improving skin and eye health and in prevention of obesity, cardiovascular disease, and diabetes [2]. Carotenoids are involved in different metabolic functions in our body. Carotenoids of the retina: Lutein and zeaxanthin act as photo protectants protecting retina from degeneration [3]. Carotenoids protect biomembranes from oxidative damage due to its antioxidant properties and their effect on biomembranes has been studied by using several techniques such as Nuclear Magnetic Resonance, X-ray diffractometry, Electron Paramagnetic Resonance, monomolecular layer technique and Differential Scanning Calorimetry [4]. Due to antioxidant property of carotenoids, they have their role in minimizing the risk of oxidative stress-mediated cardiovascular disease [5]. Carotenoids also have their role in decreasing the carcinogenesis such as Beta-carotene is involved in reducing the propagation of prostate cancer cells [6].Vitamin A is converted into its biologically active form within the body when it is absorbed and transported to the site of action. Derivatives of Vitamin A (Retinoids) show many effects on cell differentiation [7]. Carotenoids can be used to treat certain diseases.

## II. SOURCES OF CAROTENOIDS

Carotenoids are a family of red, orange and yellow pigments found in fungi, bacteria, plants and algae [8]. Human diet also contains a large number of carotenoids, with food such as vegetables and fruits containing rich pigmentation [9]. A large number of carotenoids are recognized in green vegetables and fruits [10]. In the leaves, fruits, shoots, flower, roots and seeds of the crop plants, the carotenoids are present in ample amount [11]. β- Cryptoxanthin, zeaxanthin, lycopene, lutein, α-carotene, xanthophyll and β-carotene are mainly present in our diet and these are oxygen containing carotenoids [12]. In pumpkin, collard greens, and carrotsβ- carotene and α-carotene are found [13]. Red bell pepper, pumpkin, papayas are rich source of β-cryptoxanthin [14]. Egg yolk and green vegetables are main source of zeaxanthin and lutein [15]. In the United States tomato products are the primary sources of lycopene [16].

## III. BIO-AVAILABILITY OF CAROTENOIDS

Humans are not able to synthesize carotenoids therefore they depend on vegetables and fruits to supply these compounds [17]. Carotenoids are involved in absorption, transport, and metabolism [18]. While bioavailability as well as bioaccessibility are often used indistinctly. Bioavailability is the ability of a substance or nutrient to be ingested and assimilated by the body [19, 20]. Carotenoids show physiological effects in the human body when ingested and carried to bloodstream [21]. In the normal state of plasma, carotenoids reach about 1% of the body's carotenoids content, and the excessive amount can be present in liver [22]. When lipid soluble carotenoids are taken from fatty food, they are absorbed a lot better. But the quantity of fat needed is almost 3-5 gram per meal [23]. Once taken from plasma, first appear in chylomicron fractions and VLDL and then in HDL and LDL [24].

## IV. CAROTENOIDS ROLE IN CANCER

Fat soluble compounds significantly present in nature especially in fruits and vegetables. They display significant role in different metabolic pathways in human body. One of its significant properties is antioxidant property that protects cells from damage of singlet oxygen and free radicals, increasing the immunity and preventing from the different types of cancer [25].Carotenoids decrease risk of different chronic diseases such as cancer, thus, they have important biological roles in both in human health and disease [26].

### Breast Cancer

Previous studies showed that the growth of estrogen receptor- positive tumor lines was suppressed by N-(4-hydroxyphenyl) retinamide and retinoic acid, whereas, growth of ER- tumor lines was suppressed by 4-oxoretinol [27]. Retinol and retinoic acid halt the growth of ZR-75-B, MCF-7 and Hs578T cell lines [28]. Consumption of specific carotenoids like zeaxanthin β-carotene, α-carotene and β-cryptoxanthin are inversely linked to the threat of breast cancer [29].

Crocin and crocetin are important biologically active carotenoids of saffron and they suppress tumor growth and cause the cancer cell death, due to their antioxidant and anti-angiogenic property [30].

### Prostate Cancer

In 1982, a study was designed to determine the link between plasma concentration of lycopene and possibility of prostate cancer and results concurred that the increased intake of lycopene-containing foods might decrease the propagation of prostate cancer [31].

Previous studies showed that lycopene amends the expression of apoptosis and growth-related biomarkers in prostate cancer (PC-3) cells. Along with chemotherapeutic agents and peroxisome proliferator-activated receptor gamma (PPARγ) agonists, lycopene cause cell death by necrosis and apoptosis on prostate cancer [32].

### Lung Cancer

Previous studies revealed that carotenoids prevent plasma membrane lipid oxidation because of their antioxidant properties. Carotenoids stop neoplastic transformationinduced by carcinogens. Thus, carotenoids prevent humans from cancer [33].

### Gastric Cancer

High intake of fruits may lessen the risk of gastric cancer because fruits contain important and biologically active carotenoids [34].

Lycopene halts the expression of cyclooxygenase-2 and epidermal growth factor receptor (EGFR) in the gastric cancer cells and thus it hinders the propagation of gastric cancer cells. In conclusion, ingesting lycopene-enriched diet could lower the incidence of gastric cancer [35].

## V. CAROTENOIDS ROLE IN CARDIOVASCULAR DISEASES

Cardiovascular disease (CVD) is the second most common reason of death throughout the world after cancer [36]. Inflammation in addition to the oxidative stress are major contributing factors to pathophysiology of cardiovascular diseases (CVD) [37]. In this respect consumption of antioxidant rich vegetables and fruits can be protective against cardiovascular disease [38]. Lifestyle plays a crucial role in preventing chronic inflammatory disorders especially cardiovascular disease [39, 40]. The Homeostatic balance between the reactive oxygen species (ROS) and the nitric oxide trigger the normal endothelial functions [41, 42]. Oxidative stress caused by reactive oxygen species (ROS) produce oxidized LDL, underlying disorder leading to cardiovascular diseases [43]. Various experiment revealed that carotenoids reduce the oxidative stress and inflammation [44]. So, many scientific studies revealed that carotenoids rich food reduces the cardiovascular diseases [45]. Many carotenoids like β-cryptoxanthin lutein, lycopene, Astaxanthin, zeaxanthin, and β-carotene are concerned in averting cardiovascular disease by decreasing high density lipoprotein (HDL) and oxidizing the low density lipoprotein (LDL) [46]. They also lessen the C-reactive protein (CRP) which shows significant role in cardiovascular problems [47]. A previous study showed that when high fat diet (HFD) treated rats were given carotenoids rich microalgae Dunaliella salina in their diet, the results showed that improvement in the carotenoids function [48]. This medication causes the improvement in cardiac biomarkers, congestion of myocardial blood vessels and attenuate fibrotic cardiac tissue [49, 50]. Carotenoids present in algae act as anti-inflammatory and antioxidant agents [51].

## VI. ANTI-VIRAL ACTIVITY OF CAROTENOIDS

Viruses cause several diseases and various kinds of infection. Carotenoid possess antiviral activity, and it has the potential to avert the HCV RNA as well as HBV DNA polymerase, as a result the replication of both HBV and HCV suppress [52]. The novel findings suggest that carotenoids C50 of haloalkaliphilic archaeon natrialba sp. M6 can be utilized in the treatment of antiviral diseases such as hepatitis [53]. In the old civilization, Microalgae have been utilized as food in South America, Asia and Africa for centuries. Pressurized liquid extraction (PLE) has been adapted to get antiviral compounds from microalgae generally utilized as sources of carotenoids (Dunaliella salina and Haematococcuspluvialis). The pressurized liquid extraction of D. salina and H. pluvialis manifest antiviral effects against the herpes simplex virus type 1 (HSV-1). The results showed that the extracts of Dunaliella salina were less efficacious than Haematococcuspluvialis against (HSV-1) intracellular replication [54].

## VII. ANTIBACTRIAL ACTIVITY OF CAROTENOIDS

Billions of bacteria are present in our environment and they cause bacterial diseases and infections. Carotenoids differ in colour red, orange and yellow possess antibacterial activities [55]. Flesh as well as coelomic fluids of three species of Holothuria (H. atra, H. scabra and H. leucospilota) were recognized against several bacteria Pseudomonas aeruginosa, Streptococcus faecalis, Staphylococcus aureus, Vibrio damsela. Results detected that some species were not capable to grow in the presence of these carotenoids. So, halobacterial carotenoids (β-cryptoxanthin, Xanthophyll and β-carotene) used as antibiotics against bacterial diseases [56].

## VIII. CAROTENOIDS ROLE IN NEURODEGENERATIVE DISEASES

The onset of neurodegenerative disease is a consequence of abnormal conformational changes of proteins [57]. Alterations in the biochemical homeostasis of nervous system due to oxidative stress, mental deposition, disturbance in amyloid and cholinesterase formation are associated with the initiation and progression of neurodegenerative disorders [58]. Carotenoids possess anti oxidative, anti-inflammatory and neuroprotective properties [59]. Carotenoids hinder the neurodegenerative diseases viz Huntington's disease, Parkinson's disease, Alzheimer's disease, dementia, or various mood disorders [60]. They act on these disorders possibly by modifying the action and metabolism of neurotransmitters. They act by modulating calcium signalling [61]. Carotenoid exerts positive effect on CNS.Lycopene as well as astaxanthins are still harmless at elevated concentration. Astaxanthin is a dietary supplement which has the potential to cross the blood brain barrier without remarkable adverse effect. It has higher antioxidant capability than the other carotenoids neuroprotective activity against β- amyloid toxicity [62].

Lycopene is very famous carotenoids which possess antioxidant properties, lessen blood pressure in patients of hypertension and manifest a neuroprotective profile in CNS [63].β-carotene bind to the active site of CAMKIV (important factor in neurodegenerative disorders) with high affinity, and form a stable complex, hence minimizing activity of CAMKIV [64]. Crocetin and crocin are beneficial compound of saffron which has been used for the cure of oedema, depression, cramps, and hepatic disorders in homeopathic medicine [65]. They have antitumor, antiproliferative, antioxidant, anti-inflammatory, antiapoptotic and hepatoprotective effects [66]. Thus, it is advantageous for human health to include these carotenoids in the daily meal.

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## IX. CAROTENOIDS ROLE IN TUBERCULOSIS

Mycobacterium tuberculosis the causative agent of Tuberculosis (TB) is a dreadful pathogen that spread across any organ or tissue of the body apart from damaging the lungs [67]. Malnutrition is also associated with an increased risk of tuberculosis [68]. So dietary intake of carotenoids and vitamins were used in energy adjustment method in the nutrient density model [69].The unsaturated fatty acids like linoleic acid, myristic acid, lauric acid, and oleic acid were found to be the major antimycobacterial compounds against multidrug resistance (MDR) strains of Mycobacterium tuberculosis [70]. Effective antioxidants such as carotenoids would be an effective treatment for tuberculosis where oxidative stress boosts up. Previous studies detected that high consumption of carotenoids except lutein remarkably linked with minimized the risk of active TB [71]. Several experiments on biomass of Chlorella vulgaris found that carotenoids act as an anti-TB agent [72]. Chlorella vulgarisisused as human food source and possess anti-TB activity because chlorella vulgaris has diminished hyperglycaemia and hyperlipidaemia, and exhibited protection against cancer, oxidative stress and chronic obstructive pulmonary disease [73].

## X. CAROTENOIDS ROLE IN OPTHALMIC INFECTIONS

Vitamin A exhibit important effect in eye health and its deficiency cause night blindness but this can be averted by taking a proper dose of carotenoids because 10% carotenoids can be categorized as vitamin A [74]. Low level of carotenoids increases the risk of eye disorders by change in molecular pigment optical density (MPOD), a marker of eye health. Functional food like fruits, vegetables, egg yolk, maize enriched with fat soluble carotenoids protect the eye [75]. Such as zeaxanthin, lutein and meso-zeaxanthin are the only carotenoids present in muscular pigment of retina and they could protect the retina by blue light filtering because of antioxidant properties of carotenoids and scavenges the free radicles from retina [76]. So, it revealed that the consumption of zeaxanthin or lutein but no other carotenoids such as α-carotene, β-cryptoxanthin, lycopene and β-carotene considerably minimized the risk of cataract [77]. Moreover, they can also protect against age related muscular degeneration and cataracts in eyes [78]. Ocular infection if not treated can harm the eye structure with possible visual impairment and blindness. According to research the carotenoids of Halomonas sp. might be used against antibiotic resistant and ophthalmic bacterial pathogens [56]. Bacteria are related with several types of ocular infections for example Staphylococcus aureus can cause infection named endophthalmitisin the inner chamber of the eye [79] whereasP. aeruginosa and S. pyogenes in blepharitis and E. coli in Conjunctivitis. Both gram negative and Gram positive bacteria are involved in ophthalmological infections, but gram positive bacteriamajorly contributed in ocular infections [80].Hence, carotenoids might be used to cure eye infection caused by bacteria.

## XI. ANTI HYPERGLYCEMIC PROPERTY OF CAROTENOIDS

Oxidative stress, pro- inflammatory cytokines, lifestyle factors such as sleep disturbance, high fat diet and lack of physical activity are responsible for hyperglycaemia [81]. Free radical production (oxidative stress) increase the resistance to insulin and impairs insulin secretion. During this immune system causes peripheral insulin resistance and pancreatic islet inflammation via release of cytokines and chemokines [82]. This condition could be recovered by Plant secondary metabolites such as carotenoids with anti-inflammatory and antioxidant properties. Carotenoids prevent oxidative stress and adjust the immune system by decreasing cytokines as well as chemokines. Carotenoids have been used in the treatment and protection against diabetes mellitus (DM) [83]. Previous studies disclosed that carotenoids decrease risk of type 2 diabetes in men and women [84]. There is an inverse correlation between diabetes mellitus incidence and plasma carotenoid concentration [85]. Bixin, fucoxanthin and astaxanthins are the carotenoids which decreases the sugar level in the plasma through initiation of PPARγ expression. Plasma carotenoids level and insulin sensitivity directly related to each other. Bixin plus crocin diminish the resistance to insulin via induction of PPARγ expression and the suppression of inhibitor of nuclear factor kappa B kinase subunit beta (IKKβ) and c-Jun N-terminal kinase (JNK) [86].

Current findings have disclosed the shielding role of carotenoids (lutein, zeaxanthin, and lycopene) against diabetic retinopathy [87]. Lutein shows protruding role in the protection against retinopathy. It enhances the inflammation by hindrance of FKN, MCP-1, NF-kB, and ICAM-1 in retina [88]. Carotenoids including crocin

(Hypoglycaemic effects), lycopene and astaxanthins protect oxidative stress induced neuropathy that is the major problem of diabetes mellitus [89]. Lycopene and crocin are the carotenoids which have the potential to lower the biomarkers of diabetic nephropathy including creatinine and BUN [90]. While astaxanthin lowers some of the biomarkers of diabetic nephropathy including 8-hydroxydeoxyguanosine and urinary albumin [91].

## XII. CONCLUSION

From above discussion, we can conclude that carotenoids are beneficial biological compounds which help to prevent different diseases and can also be used to treat them. Certain diseases such as hypertension, depression, cardiovascular and eye disease can be treated by carotenoids [92].Carotenoids can be marketed as pharmaceutical, nutraceutical and antioxidant products [93].Carotenoids are antioxidants which protect our cells and tissues from UV radiations. Further research is needed to study carotenoid's potential.

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