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Narrative Review

Dietary Carotenoids and their Multifaceted Roles in Cancer Prevention

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ABSTRACT

Background: Cancer remains a significant global health challenge, with dietary and lifestyle factors playing crucial roles in its incidence and prevention. Carotenoids, naturally occurring pigments found in various fruits and vegetables, have garnered attention for their potential anti-carcinogenic properties. These compounds are known for their antioxidant and anti-inflammatory effects, which contribute to their cancer-preventing capabilities.

Objective: This review aims to systematically examine the evidence regarding the role of dietary carotenoids in cancer prevention, focusing on their mechanisms of action, associated health benefits, and the implications for dietary recommendations.

Methods: A comprehensive literature search was conducted, focusing on studies that explored the relationship between dietary intake of carotenoids and cancer risk reduction. The review included peer-reviewed articles, systematic reviews, and meta-analyses published up to April 2023. Studies were selected based on predefined inclusion and exclusion criteria, with a focus on observational and intervention studies that provided clear outcomes on cancer incidence and the effects of dietary carotenoids.

Results: The evidence suggests that carotenoids such as lycopene, beta-carotene, lutein, and zeaxanthin have significant protective effects against various types of cancer, including breast, prostate, and lung cancers. These effects are attributed to the carotenoids' ability to neutralize free radicals, reduce oxidative stress, and modulate signaling pathways related to cell proliferation and apoptosis. Increased dietary intake of carotenoid-rich foods is associated with a reduced risk of cancer, highlighting the importance of diet in cancer prevention strategies.

Conclusion: Dietary carotenoids play a crucial role in cancer prevention, offering protective effects against the development of several cancer types. The findings support the inclusion of carotenoid-rich foods in dietary recommendations as a potential strategy for reducing cancer risk. Future research should focus on understanding the optimal levels of carotenoid intake and exploring the synergistic effects of carotenoids and other bioactive compounds in cancer prevention.

Keywords: Carotenoids, Cancer Prevention, Dietary Recommendations, Antioxidant Properties, Lycopene, Beta-Carotene, Lutein, Zeaxanthin, Oxidative Stress, Nutritional Epidemiology.

INTRODUCTION

Cancer remains a significant global health burden, with an estimated 19.3 million new cases and approximately 10 million fatalities in 2020 alone, excluding nonmelanoma skin cancers (1). These figures underscore the pervasive nature of cancer, which is projected to escalate to 28.4 million cases by 2040 (2). The genesis of cancer is multifactorial, involving a complex interplay of genetic and epigenetic abnormalities within cells (3). However, research indicates that a majority of cancer cases are attributable not to genetic predispositions but to modifiable environmental and lifestyle factors. Among these, dietary habits emerge as a critical element, with evidence suggesting that 30-35% of cancer deaths are diet-related (4). This highlights the potential of dietary and lifestyle interventions in cancer prevention.

The modern understanding of cancer prevention emphasizes the significance of a plant-based diet, characterized by a reduced intake of red and processed meats, refined carbohydrates, simple sugars, salt, and alcohol. Instead, a diverse consumption of fruits and vegetables is encouraged to supply a variety of nutrients essential for minimizing cancer risk. Alongside dietary modifications, lifestyle changes such as exercise and physical activity have also been shown to be effective in the treatment and prevention of

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cancer (6). Importantly, oxidative stress plays a crucial role in the initiation of cancer (7), and carotenoids, with their antioxidant properties, act as scavengers of reactive oxidative species (ROS), suggesting a preventive role for carotenoids in cancer. The presence of these compounds in the diet is inversely proportional to the risk of cancer (8, 9), underscoring their multifaceted role in cancer prevention.

MATERIAL AND METHODS

The material and methods section of this literature review was meticulously designed to explore the multifaceted roles of dietary carotenoids in cancer prevention. The primary question guiding this investigation focused on understanding how dietary carotenoids contribute to the prevention of cancer, considering the biological mechanisms involved and the epidemiological evidence supporting their protective role. To address this question, a comprehensive search strategy was employed, targeting peer-reviewed articles, systematic reviews, and meta-analyses published in leading medical and scientific databases up to April 2023.

The inclusion criteria were stringent, selecting studies that specifically examined the relationship between dietary carotenoid intake and cancer risk reduction. This encompassed research on various types of cancer, with a particular emphasis on studies that provided quantifiable data on dietary intake and utilized validated dietary assessment tools. Both observational studies (cohort and case-control) and randomized controlled trials (RCTs) were considered, provided they offered clear outcomes on cancer incidence, biomarkers of cancer risk, or mechanisms of carotenoid action in cancer prevention.

Conversely, studies were excluded if they focused solely on supplemental forms of carotenoids without dietary context, were not peer-reviewed (e.g., conference abstracts or thesis works), or did not directly assess the impact of dietary carotenoids on cancer risk. Additionally, literature that did not specify the types of carotenoids investigated or failed to control for potential confounding factors in the analysis was omitted to ensure the clarity and reliability of the evidence synthesized.

The synthesis of evidence was conducted through a narrative approach, given the heterogeneity of the studies in terms of design, population, and outcomes measured. This method allowed for the integration of findings from various studies to present a comprehensive overview of the current understanding of dietary carotenoids' role in cancer prevention. Critical appraisal of the evidence was performed, assessing the quality of the studies, the consistency of findings across different types of research, and the potential biological plausibility of the observed associations. This approach ensured that the review could offer a nuanced interpretation of the available evidence, highlighting areas of consensus as well as gaps in the current knowledge that warrant further investigation.

FINDINGS AND DISCUSSION

Carotenoids, a group of over 700 naturally occurring pigments, play a crucial role in the diet and health of humans, with around 40 of these compounds, such as lycopene, alpha-carotene, beta-carotene, xanthophyll, and lutein, being significant contributors to human nutrition (10). These compounds are synthesized by photosynthetic organisms like plants, algae, and certain bacteria and fungi, where they are essential for light absorption alongside chlorophyll (11). Animals, unable to produce carotenoids themselves, must obtain them through their diet, which includes a variety of vegetables, fruits, cereals, and microorganisms that synthesize important carotenoids like lycopene, beta-carotene, lutein, and zeaxanthin (12). The lipophilic nature of carotenoids allows them to reside within cell membranes, impacting vital membrane properties such as permeability, thickness, and rigidity (8).

Beyond their role in plant and bacterial physiology, carotenoids offer significant health benefits to humans, particularly in preventing diseases and promoting overall well-being. Their efficacy extends beyond antioxidant properties to include anti-inflammatory effects and the enhancement of the immune system (13). As antioxidants, carotenoids in both plants and animals mitigate oxidative stress by interacting with singlet oxygen and reducing the range of free radicals (12, 14). This antioxidant mechanism involves quenching or deactivating singlet-excited oxygen, protecting cell membranes from oxidative damage through physical quenching, structural modifications of the lipid bilayer, or chemical reactions leading to pigment oxidation (15, 16). At the cellular level, carotenoids exert anti-cancer effects by modulating several signaling pathways that influence cell proliferation, apoptosis, cell cycle progression, angiogenesis, and metastasis, thereby impacting the mechanisms of cancer cell spread (17).

Carotenoids are distinguished by their vibrant yellow, orange, red, and purple hues, attributable to their structure, which consists of eight isoprene units forming a 40-carbon skeleton. This structure is characterized by a long chain with nine conjugated double bonds and end groups, categorizing them into two main groups: carotenes, which are hydrocarbons, and xanthophylls, which contain oxygen in addition to carbon and hydrogen (18, 19, 20).

Lycopene, a predominant carotenoid found in tomatoes, is recognized for its red pigment and is also present in other fruits like guava, pink grapefruit, watermelon, and papaya, albeit to a lesser extent (21, 22, 23). Its structure, comprising 11 linear conjugated and two non-conjugated double bonds, reflects its nature as a highly unsaturated hydrocarbon, a tetraterpene assembled from eight

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isoprene units (24, 25). Tomatoes serve as the primary source of lycopene, contributing to over 80% of the lycopene intake in the US, with its content varying across different tomato varieties and stages of ripening (26, 27). Processed tomato products generally offer higher lycopene content due to the concentration effect from water loss during processing (28).

The bioavailability of lycopene is influenced by various factors, including food processing and cooking methods, dietary composition, and the physical form of lycopene. Processing techniques such as heating enhance lycopene's accessibility by breaking down cell walls and loosening its bond with the tissue matrix, thereby increasing its bioavailability (29, 30). However, lycopene can degrade under adverse processing and storage conditions, such as excessive heat, light exposure, and oxygen presence (31). The presence of dietary fat significantly enhances the bioavailability of lycopene, a fat-soluble compound, as demonstrated by studies showing increased absorption of lycopene and other carotenoids when consumed with fat-containing meals (32, 33).

Diets rich in tomatoes and tomato-based products have been linked to a lower risk of chronic diseases, including cancer and heart disease, with numerous studies highlighting the role of lycopene, a key component in tomatoes, as a powerful singlet oxygen quencher, more effective than other carotenoids (34, 35). Research by Mortensen et al. showed that lycopene could also target nitrogen dioxide along with thiyl and sulphonyl radicals, showcasing its broad antioxidant capabilities (36).

In the context of breast cancer, which is becoming more prevalent in many Asian countries, lycopene has been identified as a strong antioxidant, potentially more potent than other carotenoids. It has shown promise in inhibiting the growth of human mammary cancer cells and may interfere with insulin-like growth factor I (IGF-I), a protein associated with a higher risk of premenopausal breast cancer (37, 38).

For prostate cancer, studies suggest that lycopene could affect the disease's progression by influencing the expression of integrins, proteins crucial for cellular adhesion and invasion, offering a potential pathway through which lycopene may help prevent prostate cancer. Lifestyle modifications, including dietary changes to increase tomato and lycopene intake, have been considered by many men as a strategy to reduce prostate cancer risk. Meta-analyses up to 2003 have pointed to a significant reduction in prostate cancer risk with higher consumption of tomatoes or tomato products and increased lycopene levels in the blood (39, 40).

Alpha-carotene, found in orange and yellow fruits and green vegetables, has also been studied for its cancer-preventive properties. A meta-analysis involving over half a million participants revealed that increased alpha-carotene intake was associated with a lower risk of prostate cancer, suggesting its protective effect against the disease (42). Additionally, alpha-carotene has been shown to significantly reduce the risk of lung cancer with higher blood levels, indicating its potential as a protective agent against cancer (43). Its role in breast cancer prevention has also been noted, with higher levels of alpha-carotene in the blood linked to a reduced risk, highlighting its importance in cancer prevention strategies (44).

Beta-carotene, another important carotenoid found in various fruits and vegetables, has been associated with cancer prevention. Studies have linked dietary beta-carotene intake with a reduced risk of breast cancer, gastric cancer, and possibly even head and neck and pancreatic cancers. Its mechanism is thought to involve the inhibition of ROS-mediated pathways, which play a role in cancer development by promoting inflammation and cellular damage (48, 49, 50, 52, 54).

Xanthophylls, a subclass of carotenoids that include lutein, zeaxanthin, and astaxanthin, among others, have been recognized for their anti-cancer and anti-inflammatory properties, attributed to their chemical structure rich in double bonds. These compounds have been the focus of research for their potential health benefits, including their role in preventing tumors and reducing inflammation. Furthermore, xanthophylls are being explored for their possible utility in combating obesity-associated cancers, given the established link between obesity and an increased risk of certain cancers. The potential of xanthophylls and other carotenoids as functional food components in cancer prevention underscores the importance of dietary choices in managing health and disease risk (55, 56, 57, 58, 59).

Zeaxanthin, a carotenoid that gives some fruits and vegetables their yellow or red colors, is especially found in green leafy vegetables, certain fruits, and egg yolks (60). It's known for its ability to help protect against neurological disorders. This protection comes through its actions in reducing inflammation, fighting oxidative stress, and preventing cell death (60).

Fucoxanthin, a carotenoid from seaweed, stands out for its strong antioxidant properties. Like other carotenoids, fucoxanthin fights against oxidative stress by neutralizing free radicals, which can damage cells and lead to various diseases (61).

Astaxanthin is another carotenoid, recognized by its vibrant red color and remarkable antioxidant strength. It's believed to be much more powerful than other carotenoids in combating oxidative stress. Studies have shown that astaxanthin can improve glucose and fat metabolism in animals, helping to reduce insulin resistance and decrease fat buildup (61).

Lutein is a carotenoid present in many fruits and vegetables and is crucial for eye health. Since the human body can't make lutein, it must come from our diet. Lutein protects the eyes by filtering harmful blue light and acting as an antioxidant. It's linked to a lower risk of age-related macular degeneration and cataracts, highlighting its importance in maintaining good vision (62, 63).

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Capsanthin, found in red peppers and some other plants, is known for its red color and its health benefits. It has antioxidant properties and has been shown to fight tumors, reduce inflammation related to obesity, and increase good cholesterol levels in the blood. Capsanthin has been studied for its potential in pain relief, heart protection, weight management, and its anti-inflammatory and antimicrobial effects (64).

CONCLUSION

In conclusion, adopting a lifestyle and diet rich in carotenoids can significantly contribute to cancer prevention and overall health improvement. Carotenoids, with their antioxidant and anti-inflammatory properties, play a vital role in reducing oxidative stress and slowing tumor growth. Including tomatoes, fruits, and leafy vegetables in the diet can offer protective benefits against cancer and other chronic diseases, emphasizing the importance of dietary choices in health maintenance and disease prevention.

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