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Review Article

Lycopene and Oral Health: A Comprehensive Review.

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ABSTRACT

Lycopene, a carotenoid pigment predominantly found in tomatoes and other red fruits, has garnered attention for its potential health benefits, particularly concerning oral health. This abstract explores the role of lycopene in oral health, focusing on its antioxidant properties, anti-inflammatory effects, and its ability to combat oral diseases. Recent studies suggest that lycopene may inhibit the growth of pathogenic bacteria and reduce the risk of periodontal disease, dental caries, and oral cancers. Furthermore, its contributions to salivary health and mucosal integrity highlight lycopene as a promising agent in dental hygiene and preventive dentistry. This review aims to synthesize existing literature on lycopene's effects on oral health, revealing its potential in fostering better dental outcomes and guiding future research directions in this domain.

Keywords: Lycopene, Oral Health, Dentistry.

Introduction

Oral health is a critical component of overall health, influencing aspects such as nutrition, communication, and quality of life. Poor oral hygiene can lead to various conditions, including dental caries, periodontal disease, and oral cancers, which pose substantial public health challenges. Emerging research highlights the significance of dietary components in enhancing oral health, with phytonutrients gaining attention for their protective properties. Among these, lycopene stands out due to its abundant presence in tomato products and several other fruits and vegetables.[1]

Lycopene is a potent antioxidant known for its ability to neutralize free radicals, thereby potentially reducing oxidative stress in oral tissues. Its anti-inflammatory characteristics can contribute to periodontal health, while its antimicrobial activities may help inhibit the growth of harmful oral bacteria. Moreover, the influence of lycopene on salivary flow and composition could further support oral health by enhancing the natural defense mechanisms of the oral cavity.[1,2]

This introduction serves to contextualize the interest in lycopene as a non-traditional dental care agent and establishes the foundation for a detailed examination of its biological effects on oral health. By synthesizing existing research and identifying knowledge gaps, we aim to foster a better understanding of lycopene's role in preventive and therapeutic dental care.

Based on their chemical structure, carotenoids are broadly classified into two categories:[2-4]

Carotenes: These carotenoids are purely hydrocarbons. Well-known examples are β-carotene and lycopene.

Xanthophylls: These compounds are oxygenated derivatives of hydrocarbons. They include zeaxanthin and lutein (hydroxy derivatives), spirilloxanthin (methoxy derivative), echinenone (oxo derivative), and antheraxanthin (epoxy derivative).

Highlighting the diversity of carotenoids, lycopene is a significant fat-soluble carotenoid discovered in 1959. It is most prevalent in red fruits and vegetables, as well as in certain algae and fungi. Among these, tomatoes and tomato-based products such as sauces and ketchup are major dietary sources of lycopene, offering higher concentrations compared to raw or unprocessed tomatoes. Other fruits that contain lycopene and contribute to its dietary presence include apricots, cranberries, grapes, pink grapefruit, guava, papayas, peaches, and watermelons.

Carotenoids' contributions extend beyond their vivid hues and nutritional benefits; they are essential elements of nature and human health. Their roles underscore their significance in the biological tapestry, emphasizing the intricate connections between appearance and functionality in living organisms.

Dietary source of Lycopene: Lycopene is a powerful antioxidant found in various red and pink fruits and vegetables. Here are some of the primary dietary sources of lycopene:

Tomatoes: Both fresh and processed forms like tomato paste, sauce, and ketchup are rich in lycopene. Cooked or processed tomatoes often provide more readily absorbable lycopene.

Watermelon: This refreshing fruit is another excellent source, with a sweet flavor packed with lycopene.

Pink Grapefruit: Offers a tangy taste along with lycopene content, contributing to your antioxidant intake.

Guava: Known for its tropical flavor, guava provides a substantial amount of lycopene.

Papaya: This tropical fruit delivers a healthy dose of the antioxidant.

Red Bell Peppers: Though less than the fruits listed above, they still contribute to lycopene intake.

Apricots and Red Cabbage: These contain smaller amounts but are still notable sources.

Lycopene and Health: Lycopene, a powerful antioxidant found in tomatoes and other red fruits, is associated with numerous health benefits, largely due to its ability to neutralize harmful free radicals in the body. Here's how lycopene contributes to general health:

Cardiovascular Health: Lycopene is linked with reduced risk of heart disease by lowering LDL cholesterol levels and improving blood vessel function. It helps maintain healthy blood pressure and reduces inflammation, contributing to overall heart health.

Cancer Prevention: Observational studies suggest that a diet rich in lycopene-containing foods may lower

the risk of certain types of cancer, particularly prostate cancer. Its role in inhibiting cancer cell growth and proliferation, as well as preventing DNA damage, underscores its potential as a cancer-fighting nutrient.

Eye Health: Lycopene's antioxidant properties support eye health by protecting against oxidative stress which can lead to cataracts and age-related macular degeneration.

Skin Protection: By combating the harmful effects of UV rays, lycopene helps protect the skin from sunburn and may have an anti-aging effect due to reduced sun-induced damage.

Bone Health: Some research indicates that lycopene may contribute to bone health by reducing oxidative stress on bone cells, thus potentially preventing bone-related diseases such as osteoporosis.

Neurological Health: Its antioxidant effects may play a role in protecting the brain against age-related cognitive decline by reducing oxidative damage and inflammation in brain cells.

Immune System Support: By enhancing the body's natural defenses, lycopene helps strengthen the immune system, making it more effective at fighting infections.

Metabolic Health: There's evidence that lycopene may have beneficial effects on metabolic health by improving insulin sensitivity and lowering blood sugar levels, which is particularly beneficial in the management of diabetes.

To harness these benefits, incorporating lycopene-rich foods like tomatoes, watermelon, pink grapefruit, and papaya into your diet is recommended. Lycopene is better absorbed when consumed with healthy fats, so pairing these foods with a bit of olive oil, for example, can enhance its bioavailability. Additionally, cooking foods like tomatoes can increase the body's ability to absorb lycopene.

Role of Lycopene in Oral Health[2-6]

Prevention of Oral Cancer: Neoplasm is a complex, multistage disease process in which a single cell can transform from a normal state to malignancy, ultimately potentially leading to the destruction of the tissue's foundational structure. The development of cancers involves a sequence of cellular and molecular changes. These changes can be influenced by a variety of endogenous and other free radicals, which are well-known for their mutagenic properties. Recently, these free radicals have also been identified as key mediators in the phenotypic and genotypic alterations that progress from mutation to neoplasia. As such, there is a significant belief that free radicals contribute substantially to the process of cancer development in humans.

Oral cancer ranks as one of the most prevalent malignancies worldwide and stands 12th among all cancer types. Oral squamous cell carcinoma (OSCC) emerges via a multi-step process characterized by genetic, epigenetic, and metabolic transformations triggered by carcinogenic exposures. Within these influences, the impact of diet and nutrition on preventing oral cancers has piqued substantial interest among researchers and healthcare professionals.

While early-stage neoplasia can be treated with surgery or radiotherapy, the majority of patients are diagnosed during advanced stages, where treatment outcomes have not significantly improved in recent years. Consequently, reducing the incidence of this disease may be feasible through preventive strategies. These strategies aim to suppress, reverse, or prevent premalignant lesions from forming and progressing through the multistep initiation, promotion, and progression processes into OSCC.

Lycopene has been proposed as a potential agent in preventing carcinogenesis and atherogenesis by safeguarding vital cellular biomolecules such as lipids, lipoproteins, proteins, and DNA. Research has demonstrated the anticancer properties of lycopene in both in vitro and in vivo tumor models. The mechanisms behind lycopene's inhibitory effects on carcinogenesis may involve the modulation of reactive oxygen species (ROS) and other oxidative stress pathways, thus offering a protective role against cellular damage.

Lycopene in OSMF: Oral submucous fibrosis (OSMF) is a chronic condition characterized by progressive scarring in the oral cavity. It is primarily seen in individuals of South-East Asian descent. The origins of OSMF are complex and involve multiple factors. Excessive consumption of chili, genetic predisposition, autoimmune issues, and deficiencies in iron and vitamins all contribute to its development. However, a significant link has been established between OSMF and the chewing of areca nut and pan masala.

Research has demonstrated that extracts from the areca nut can promote the synthesis of collagen in human skin cells, thereby strengthening collagen fibers and making them resistant to breakdown by collagenase, which leads to the development of fibrosis. Furthermore, areca nuts contain traces of copper, which is known to enhance collagen production by increasing lysyl oxidase activity. This enzyme plays a critical role in the synthesis and cross-linking of collagen.

OSMF shares behavioral and malignant transformation traits with other precancerous conditions of the oral cavity. Consequently, it is believed that therapeutic interventions used in other oral precancers could also prevent or reverse OSMF. Many researchers advocate for the use of conservative treatments over traditional methods. This includes avoiding potentially harmful treatments like injections of steroids, hyaluronidase, and placental extracts.

There is evidence from human studies that antioxidant (AO) treatments may help prevent cancer. However, oral intake of retinoids, a type of antioxidant, can have significant toxic effects on healthy tissue. Carotenoids, a less toxic class of micronutrients, hold promise in OSMF management, with lycopene noted for its potential benefits. Lycopene may enhance immune responses or act directly on tumor cells to exert its effects. Studies, such as one by Kitade et al., have shown that lycopene can inhibit liver fibrosis in rats, and it is believed to work similarly in impeding the fibrotic activity of abnormal fibroblasts in OSMF. Additionally, lycopene appears to promote healthier cellular activity in the disease process.

Lycopene in Aphthous Ulcer: Lycopene, a potent antioxidant predominantly found in tomatoes, may play a beneficial role in managing aphthous ulcers, or canker sores. Although the exact causes of these ulcers are not fully understood, stress, nutritional deficiencies, and autoimmune responses are thought to be contributors. Lycopene's antioxidant properties are particularly notable, as they help diminish oxidative stress and inflammation throughout the body. This, in turn, could help soothe the inflammatory response associated with aphthous ulcers. Additionally, by neutralizing free radicals and curbing inflammation, lycopene may accelerate the healing of these ulcers, minimizing damage to nearby oral tissues. Moreover, it supports the immune system, enhancing the body's ability to defend against infections and facilitating quicker ulcer recovery. Regular consumption of lycopene-rich foods may potentially lower the frequency of ulcer outbreaks by promoting an optimal oxidative balance and sustaining immune health. While not a direct cure, including lycopene in a balanced diet could ease ulcer symptoms and support healing. It is always advisable to consult a healthcare professional for persistent or severe cases.

Lycopene in Prevention of Periodontal Diseases: The periodontal tissues provide an ideal setting to investigate how reactive oxygen species (ROS) induce tissue damage and how antioxidant (AO) defenses respond to bacterial proliferation, using noninvasive methods to collect gingival crevicular fluid. ROS inflict harm on tissues through various mechanisms, such as DNA damage, lipid peroxidation, protein degradation (including damage to gingival hyaluronic acid and proteoglycans), oxidation of vital enzymes like anti-proteases, and enhancement of pro-inflammatory cytokine release by immune cells. Despite their brief lifespans, ROS can inflict significant tissue damage by instigating free radical chain reactions. To counteract this, the body has evolved several antioxidant protective mechanisms that aim to neutralize harmful oxidants or repair tissue damage from ROS promptly as they develop.

Recommended Dose of Lycopene: There isn't a specific ideal dose for daily lycopene intake, but previous studies provide useful insights. For instance, a study showed that 6.5 mg of lycopene per day was effective in combating cancer in men. In cases of advanced prostate cancer, the dose might need to be increased to 10 mg per day. Another study found that, in elderly populations, taking 15 mg of lycopene daily for 12 weeks could enhance immune function by increasing natural killer cell activity by 28%. Consequently, it appears that different doses and durations of lycopene supplementation may be recommended for various health benefits. In line with multiple studies, a general suggestion for daily lycopene intake could range from 2 to 20 mg per day.[7-9]

Safety Concern of Lycopene: The monitoring of safety related to medicinal plants and plant-derived phytochemicals is crucial. Several studies, both in test tubes and living organisms, have examined the potential toxicity of lycopene. Research indicates that lycopene, at concentrations up to 10 μM, does not harm the viability of cultured neural cells from the rat's cerebellum. Furthermore, another study involving rat hippocampal neurons found no notable toxic effects when lycopene was introduced to these cells, even though carotenoids can sometimes exhibit pro-oxidant effects, particularly at high tissue concentrations.

In toxicological evaluations using rats, no adverse effects were observed at the highest examined dose of lycopene, which was 1.0% included in their diet. Various forms of lycopene, such as those extracted from tomatoes, synthetically produced, or in crystallized extract form, are generally considered safe for use in various food products. There are no known reports of negative effects from consuming lycopene at standard or typical doses. In human studies, the no-observed-adverse-effect level for lycopene is cited as 3 grams per kilogram of body weight per day, with actual daily intake estimated to be significantly lower. Even at the highest percentile of consumption, it remains at 123 mg per day.

However, it's important to note that high doses of lycopene might induce the expression of cytochrome P450 2E1, especially when combined with alcohol. Therefore, it is advisable to avoid high doses of lycopene when consuming alcohol concurrently. Additionally, due to lycopene's strong antioxidant properties, caution is recommended for patients undergoing chemotherapy or radiation therapy.

A unique case highlighted lycopenemia in a woman who had consumed roughly two liters of tomato juice daily for several years. This resulted in lycopene accumulation in her liver—though without apparent liver dysfunction—and an orange tint to her skin.[7-9]

Conclusion

In conclusion, lycopene emerges as a noteworthy dietary component with potential implications for oral health. Its strong antioxidant properties, coupled with anti-inflammatory and antimicrobial effects, suggest that incorporating lycopene-rich foods into the diet may benefit oral hygiene and reduce the risk of various oral diseases, including dental caries, periodontal disease, and even oral cancers. By promoting salivary health and enhancing mucosal integrity, lycopene may play a crucial role in supporting the body's natural defenses within the oral cavity.

Despite the promising findings, further research is essential to thoroughly understand the mechanisms by which lycopene affects oral health and to discern optimal dietary amounts and forms for maximum benefit. Investigating the synergistic effects of lycopene with other nutrients and its role in diverse populations can provide deeper insights into its efficacy. Public health initiatives and dental practitioners should consider

emphasizing the inclusion of lycopene-rich foods in dietary recommendations as part of a holistic approach to improving oral health outcomes. Ultimately, understanding the impact of lycopene may pave the way for innovative preventive strategies in dental care, with the potential for enhancing overall health through dietary interventions.

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