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Review Article

Antioxidants in oral medicine: A review

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ABSTRACT

The lifestyle deviations in recent past years and stress-related work regularly instigate lots of complications, like emotional and mental trauma to our body. Abusive habits like pan, gutka, supari, cigarettes add insult to it. Consequences in the release of free radicles triggering oxidative damage to cells. Leading to various diseases and disorders. Antioxidants are regularly found in many food products like leafy vegetables and fruits. Antioxidants are capable of stabilizing or deactivating, free radicals beforehand they attack cells. Antioxidants are critical for preserving optimal cellular and systemic health and well-being. High intakes of antioxidant nutrients from food sources appear to offer some health advantages. It is valuable to eat a wide variety of cereals, fruits, and vegetables rather than taking only these supplements.

1. Introduction

In routine day-to-day life work patterns and workload have been increased, causing increased work stress and leading to too many health and mental problems. Irregular work timings also add to it. With disturbed sleep patterns, it becomes more detrimental to the health of the individual.

Imbalanced food intake due to irregularity in the timings of the foods i.e., skipping breakfast or lunch many times and dinner at late night upsets the body's normal system. A lack of fruits and green leafy vegetables in the diet prevents the body from receiving natural antioxidants. The passion for eating outsides with increased junk foods does not provide any or sufficient nutrients and antioxidants. The use of coloring agents, sweetening agents, and the potential carcinogens often used in outside food makes it more hazardous for the health.

Influencing by lifestyles and by the stress of work use of tissue abusing habits are also increased. Cigarette smoking, alcohol drinking, and drugs damage their health. Habits such as Pan, Gutkha, and Supari, cause potential trauma to the oral tissues and lead to an increased risk of cancer development.

Pan, Gutkha, and Supari are commonly chewed in the Indian subcontinent. Pan is a mixture of betel nut (supari), lime, and catechu (kattha) with various flavoring agents it is being consumed by millions all over India. made of crushed areca nut (also called betel nut), tobacco, catechu, paraffin wax, slaked lime (Calcium oxide), and sweet or savory flavorings.

Antioxidants are capable of stabilizing, or deactivating, free radicals before they attack cells. Antioxidants are critical for maintaining optimal cellular and systemic health and well-being. A biological antioxidant may be defined as "a substance present in low concentrations compared to an oxidizable substrate (e.g., proteins, lipids, carbohydrates, and nucleic acids) that significantly delays or inhibits oxidation of a substrate. Antioxidants may be considered as the scavengers of free radicals".[1]

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2. Antioxidants

Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Antioxidants interact with and stabilize free radicals and may prevent some of the damage free radicals might otherwise cause. Free radical damage may lead to cancer. Examples of antioxidants include beta-carotene, lycopene, vitamins C, E, A, and other Substances (Sies, 1997).[2]

Low levels of antioxidants, or inhibition of the antioxidant enzymes, cause oxidative stress and may damage or kill cells.[3] All these factors produce oxidative stress and cause tissue damage. So as an action against all these, natural and supplemental antioxidants are necessary to prevent cell damage.[3]

3. Oxidative Damage

These unhealthy oxygen atoms are unbalanced and constitute the most common “Free Radicals” (FR).[4] In recent years the term "Reactive Oxygen Species" (ROS) or "Reactive Oxygen Intermediates" is a collective term that has been adopted to include molecules such as

1. Hydroxyl radical (OH)
2. Superoxide anion (O2)
3. Hydrogen peroxide (H2 O2)
4. Hypochlorous acid (HCIO)

All are capable of reacting with membrane lipids, nucleic acids, proteins and enzymes, and other small molecules, resulting in cellular damage. Several studies have proven that the management of premalignant lesions should include antioxidants along with the cessation of the habit. Lycopene is a powerful antioxidant obtained from tomatoes. Has been shown to have several potent anti-carcinogenic and antioxidant properties and has demonstrated profound benefits in precancerous lesions such as leukoplakia.[1,5]

Halliwell (1997) suggested that "An antioxidant is any substance that, when present even at low concentrations with those of an oxidizable substrate will significantly delay or inhibit oxidation of that substrate.” Harmful Free radicals usually arise during metabolism and sometimes the immune system cells create them to neutralize harmful pathogens.[6]

4. Use of Antioxidants

Antioxidants are widely used in dental practice for benign diseases or premalignant lesions. Free radicals seem to influence many oral diseases, most commonly periodontitis, premalignant lesions like leukoplakia, and oral cancer. A wide array of antioxidants has potential application in dental therapeutics. E.g.: Eugenol (effective in toothache), Green tea (effective in leukoplakia), and Ascorbic acid (effective in gingivitis).[7]

Dietary substitutes like beta carotene, provitamin A, vitamin A, vitamin C, vitamin E, lipoic acid, zinc, selenium, and spirulina can prevent oral cancer at a very early stage i.e., in premalignant lesions, in premalignant conditions, and also in carcinoma in situ.[8]

4.1. Therapeutic use of antioxidants for oral lesions

The possible uses of antioxidants for oral mucosal lesions include the following:

1. The prevention of lesions in high-risk individuals with mucosa clinically appears normal with no history of either premalignant or malignant lesions.
2. The treatment of premalignant oral lesions.
3. In patients who have had either premalignant or malignant oral lesions that have been successfully treated, to prevent recurrence of the treated initial lesion or to prevent the development of a second or a separate primary.[4,7]

4.2. Efficacy of a mixture of antioxidant vitamins

Individual antioxidant vitamins produce varying degrees of tumor regression only at very high doses, which frequently causes toxicity, especially with retinoid derivatives. At lower doses, they may be ineffective or stimulate the growth of cancer cells. Therefore, single vitamins in cancer treatment have no biological or clinical merit. Lower doses of individual vitamins 13-cis-retinoic acid, sodium ascorbate, d-a-tocopherol succinate, and polar carotenoids without any beta-carotene as part of a mixture can be used in cancer treatment and thereby avoid the possibility of toxicity seen with single vitamins at higher doses, or growth stimulation seen at lower doses.[2]

4.3. Sources of antioxidants:[11]

4.4. Commercially available antioxidants

There are many commercial antioxidant combinations available. Many of these are commonly used in clinical practice.[11,12]

4.5. Some antioxidant combinations used

1. Beta-carotene 30 mg + ascorbic acid 1,000 mg + alpha-tocopherol 800 I.U used in treatment of leukoplakia for 9 months.

Vitamin C is an antioxidant that goes to work on a cellular level to adjust high levels of stress hormones and enhance the function of immune cells throughout your body. Vitamin E inactivates free radicals that can harm cells. Vitamin A, a phytonutrient that works as an antioxidant, promotes immune health and protects DNA.[13,14]

The successful therapeutic manipulation of the cellular response by antioxidant molecules might necessitate the

Table 1: Carotenoids

Beta-carotene	360 mg beta-carotene/week for 12 months for treatment of leukoplakia.
Lycopene	4-8 mg/day orally for 3 months for leukoplakia.[5] 16 mg/day orally for 2 months for Oral submucous fibrosis. 8 mg/day orally for 2 weeks for Gingivitis (Lycored).[9] Atrophic/erosive oral lichen planus.

Table 2: Vitamins

L-ascorbic acid (Vitamin C)	100 mg/day for smokers.[1,10] 60 mg/day for non-smokers.[1,10]
A-tocopherol (vitamin E)	11.9-14.9 I.U. or 8-10 mg/day given orally.[1] 800 I.U./day for 2 months for leukoplakia.[10]
Retinoic acid (vitamin A)	3333 I.U. or 0.5-1 mg/kg/day 13 cis retinoic acid given orally for leukoplakia.[1] 1-2 mg/kg/day of 13 cis retinoic acids for 3 months for leukoplakia.[10]
Fenretinide (4-HPR)	Systemic use of 20 mg/day for 3 months for oral leukoplakia.

Table 3: Natural food sources of some antioxidants (Adapted from Shahidi, 1997)

Compound/Property	**Source**
Vitamin E (tocopherols & tocotrienols)	Oilseeds, vegetable oils, nuts, whole grains, cereals, margarine etc.
Vitamin C	Fruits and vegetables, berries, citrus fruits, green papers
Carotenoids	Dark leafy vegetables, carrots, sweet potatoes, tomatoes, apricots, citrus fruits, kale etc.
Flavonoids/isoflavonoids	Fruits and vegetables, oildseeds, berries, peppers, citrus fruits, tomatoes, onions etc.
Phenolic acids/derivatives	Oilseeds, cereals, grains, etc.
Catechins	Green tea, berries, certain oilseeds, etc.
Extracts/essential oils	Green tea, rosemary, sage, clove, oregano, thyme, oat, rice bran etc.

Table 4:

Capsule LICORAY	Lycopene 600mcg + Vitamin A 5000 I.U. + Vitamin C 50 mg + Vitamin E 10 mg + Zinc sulphate monohydrate 61.8 mg/Vegetable capsule.
Capsule ANTOXID/ ANTOXID-HC	Beta-carotene 10 mg, Zinc sulfate monohydrate 27.5 mg, Selenium dioxide 200 mcg, Manganese 2 mg, Copper 1 mg.
Capsule LYCORED (softgel)	Lycopene 2000 mcg, Selenium 35 mcg, Zinc 7.50 mg.
Capsule ALA-100	Alpha-lipoic acid.
Capsule C-RED	Lycopene 2000 mcg, Vitamin A 2500 I.U, Alpha-tocopheryl acetate 10 I.U, Vitamin C 50 mg, Zinc sulfate monohydrate 27.45 mg, Selenium dioxide 70 mcg.
Capsule ANTIANO	Lycopene 2000 mcg, Vitamin A 5000 I.U, Tocopheryl acetate (Vitamin E) 25 I.U, Vitamin B6 3 mg, Folic acid 1.5 mg, Copper sulfate 2 mg, Zinc sulfate 27.45 mg, Selenium dioxide 70 mcg.
Capsule ANTI – OX	Beta-carotene 10 mg, Vitamin A 5000 I.U, Vitamin C 100 mg, Vitamin E 25 mg, Copper 1 mg, Manganese 1.5 mg, Zinc 7.5 mg, selenium 150 mcg.
Capsule COTEN	Coenzyme Q-10.
Capsule COVITA	Vitamin E 100 I.U / 200 I.U.
Capsule BIO-E	Vitamin E 400 I.U.
Capsule BQ-10	Coenzyme Q – 10: 30 mg, Vitamin E 30 mg.
Capsule C – RED	Lycopene 2000 mcg, Vitamin A 2500 I.U, Alpha-tocopheryl acetate 10 I.U, Vitamin C 50 mg, Zinc sulfate monohydrate 27.5 mg, Selenium dioxide 70 mcg.
Capsule SPIRUZOX	Spirulina 500 mg.
Capsule ELDERVIT ZC	Vitamin A 2500 I.U, Vitamin C 150 mg, Vitamin E 200 I.U, Zinc 22.5 mg, Copper I mg, Selenium 40 mcg, Omega-3 fatty acid EPA 90 mg + DHA 60 mg.
Capsule BEVIT	Beta-carotene 10 mg, Vitamin C 150 mg, Vitamin E 25 mg, Selenium 75 mcg, Zinc oxide 61.8 mg.
Capsule BIO-E	Vitamin E 400 I.U.

maintenance of the critical balance between FR/ROS and antioxidant defense systems. It may be necessary to deliver anti-oxidants selectively to specific cell types and to define the concentrations suitable for blocking inappropriate cell responses but leaving the unimpaired physiological levels of FR/ROS activity necessary for normal cell function.[14]

5. Discussion

Protection against free radicals can be enhanced by an ample intake of dietary antioxidants, of which the best are Vitamin E, Vitamin C, and carotenoids. The antioxidant micronutrients are important for limiting oxidative and tissue damage and preventing increased cytokine production, resulting from prolonged activation of an immune response. Dietary and other enzymatic antioxidants protect the lipids of lipoprotein and other biomembranes against oxidative damage by intercepting oxidants before they can attack the tissues. It is important to have an adequate antioxidant intake from both diet and supplementation if needed and can be a valuable adjunct in the treatment of chronic inflammatory dental disorders.[15]

Many believe that if enough of an essential nutrient is good, then more is better. However, when large amounts of antioxidants nutrients are taken, they can also act as pro-oxidants by inducing oxidative stress.[16,17] Pro-oxidant activity can persuade either beneficial or harmful effects on the biological system.

In recent years, antioxidants and prooxidants have been extensively studied. It seems that most dietary antioxidants can behave as prooxidants; it is subject to their concentration and the nature of neighboring molecules.

The single antioxidants when applied to cells possess anti-angiogenic, anti-inflammatory, antiviral, and/or anti-tumor properties. Combined antioxidant supplements may provide greater protective effects against free-radical damage to human gingival and periodontal tissues than individual antioxidants.[18]

The knowledge of antioxidants is useful in reducing the incidence of oral cancers at the initial stages through noninvasive techniques. Recent clinical studies have shown the beneficial effects of these antioxidants in oral leukoplakia, a characteristic oral precancerous lesion.[19]

Efforts to increase the level of nutritional education are the basic necessity at present in contrast with the past as major and deadly diseases like precancerous lesions and conditions, oral cancer can be cured by just acquiring healthy habits & burden of an extravagant treatment could be downsized.[20]

Antioxidant enzymes act as a useful biomarker for various oral diseases, therefore, supplementation of antioxidants provides may reduce the prevalence of oral problems.[21]

Supplements are available that will activate the body's antioxidant production within the cells, and turn down the pro-inflammatory genes. Hence, the judicious use of antioxidants may be useful to prevent free radical-related disorders.[22]

6. Conclusion

High intakes of antioxidant nutrients from food sources appear to offer some health advantages. In addition, a diet high in fruit and vegetable often means a lower intake of fat and a higher intake of fiber, which may also protect against many diseases. Vitamin and mineral supplements do not necessarily make up for poor food habits or unhealthy lifestyle practices. It is advisable to eat a wide variety of cereals, fruits, and vegetables in a reasonable amount rather than rely on supplementation with a few antioxidants.

In routine dental practice doctors commonly encountered oral diseases and lesions. This can be managed very efficiently with a thorough knowledge of oral medicine and antioxidants.

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8. Conflict of Interest

None.

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