AN ORAL CAVITY PROTECTOR: MELATONIN- THE KNIGHT RIDER

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ABSTRACT

Melatonin is a hormone that is primarily synthesized in the pineal gland. This hormone plays a vital role in protecting oral cavity from the harmful effects caused by various pathogens, autoimmune diseases and oral cancers. This protective action of melatonin comes from its immunomodulatory, antioxidant (free radical scavenger), proliferation and synthesis of Type I collagen, bone formation, oncostatic activity which includes anti-proliferative functions, stimulation of anticancer immunity, and modulation of oncogene expression, anti-Inflammatory and anti-angiogenic effects. This article highlights the therapeutic effects of melatonin on the damages caused by mechanical, bacterial, fungal, or viral origin, in postsurgical wounds caused by tooth extractions and other oral surgeries on the oral cavity, but also on the bone formation in various autoimmune disorders such as Sjogren syndrome, in periodontal diseases, in toxic effects of dental materials, in dental implants, and in oral cancers.

KEYWORDS: Melatonin, Antioxidant, Gingivitis, Periodontitis, Candidiasis.

INTRODUCTION

Melatonin, N-acetyl-5- methoxy tryptamine is synthesized and secreted by the pinealocytes, the major cells of the pineal gland and various organs of the body. It was first isolated and
characterized in 1958,[1] although one of its actions, ability to blanch the skin of amphibians was already been shown in 1917.[2]

Pinealocytes take up tryptophan from the blood and convert it into serotonin through hydroxylation and decarboxylation. During dark period, serotonin is converted into N-acetyl serotonin by the enzyme N-acetyltransferase. N-acetyl-serotonin is methylated to form the melatonin by the enzyme hydroxyindole –O- methyltransferase. Because of its association with nighttime, melatonin is referred to as the “Chemical expression of Darkness”. [3] In mammals, including humans, melatonin reaches its maximal levels near the middle of the dark period with uniformly low levels during the day. It is highly lipophilic so it reaches every cell in the organism. It is found in high concentrations in bone marrow, intestine, and subcellular organelles, such as the nucleus and mitochondria. After its release into blood, melatonin diffuses passively in the saliva with 24% to 33% of those in plasma. Roughly 70% of the plasma melatonin is bound to albumin, and this melatonin does not enter the saliva for any appreciable extent.[4]

In this article, we consider the potential role of melatonin in the oral conditions including (1) tooth development and dental caries (2) melatonin as an anti-inflammatory agent in oral cavity (3) herpes viral infection (4) candidiasis (5) gingivitis and periodontitis (6) oral cancer (7) dental materials.

**DISCUSSION**

**Role of melatonin in oral cavity**

1. **Melatonin in tooth development and caries**

Melatonin plays a physiological role in the development and growth by regulating the cellular function of the odontogenic cells in the tooth germs.[5] In hamsters, a highly seasonal species, more caries lesions develop in the spring and summer, when the duration of nocturnal elevated melatonin is minimal, and conversely, caries occur less commonly in the autumn and winter when the melatonin levels are maximal.[6]

Because of melatonin’s antibacterial properties, its ability to reduce dental caries can be used on regular basis to reduce tooth decay. Here again, melatonin enriched toothpastes, mouth washes and dental gels may prove of value.
2. **Melatonin as an anti-inflammatory agent in oral cavity**

The antioxidant properties and free radical scavenging action of melatonin may be beneficial for the treatment of local inflammatory lesions and for fastening the healing process. It inhibits the inflammatory enzyme COX-2 by binding at the active sites.\(^7\)

This property can be therapeutically used in the oral cavity diseases such as bacterial and viral lesion, postsurgical wounds, and oral surgeries acting as a promotor of bone formation.\(^7\)

3. **Melatonin and herpes viral infection**

Herpes simplex lesions of the mucosa of the lips and oral cavity are often painful and unsightly.\(^8\) These infections are frequently exacerbated by a weakened immune system and the resulting molecular damage is often because of free radical.\(^9\)

Melatonin stimulates both, innate and adaptive immune responses and the indoleamine differentially modulates the enzymes with pro-inflammatory actions while limiting the production of inflammatory mediators including cytokines and leukotrienes. These actions coupled with free radical mechanism of melatonin and by its byproducts are consistent with its ability to resist the viral infection although it may not kill the virus.\(^8\)

4. **Candidiasis**

Melatonin reduces the level of IL-6 and shortens the time to the improvement in animals with candida sepsis. It also reduces the level of TNF-alpha and adhesion molecule in melatonin treated septic rats as compared to untreated septic rats.\(^10\)

Considering its therapeutic value it can be used in candida sepsis and antimycotic treatment because of its immune regulatory effects. Some studies support the proposal that melatonin enhances the phagocytic function as well as it also shows reduced oxidative stress originating while candidiasis.\(^11,12\)

5. **Gingivitis and Periodontitis**

Periodontal disease is very common chronic inflammatory condition. The disease state ranges from gingivitis to advanced periodontitis. In advanced periodontitis, there is extreme loss of gingival tissue and alveolar bone. Severe inflammatory responses are associated with massive free radical generation. Thus, the action of melatonin as anti-inflammatory and anti-oxidative
agents could be beneficial, particularly when placed directly into the mouth, to abate the severity of inflammation of the gingiva and periodontium.

Melatonin leads to reduced serum levels of the pro-inflammatory cytokines, interleukin-1B and tumor necrosis factor-alpha and lowers the amount of 8-hydroxy-2-deoxyguanaine in the gingival muscle tissue. It also stimulates the production of glutathione, an important intracellular antioxidant.[13]

6. Oral cancer
Melatonin exerts oncostatic activity through several biologic mechanism including anti-proliferative actions, stimulation of anticancer immunity, modulation of oncogenic expression, and anti-inflammatory, antioxidant and anti-angiogenic effects.[14]

Melatonin amplifies the antitumor activity of interleukin-2. It is one of the factors that can control cell proliferation. It is only known chronobiotic and hormonal regulatory of neoplastic cell growth. With physiological circulating concentration, melatonin is cytostatic and inhibits cancer cell proliferation.[20]

7. Dental materials
The antibacterial properties of the melatonin, has the property to reduce dental caries, which are often related to Streptococcus mutans as well as other bacteria. Melatonin shows a biocompatibility with tissues of the oral cavity and because of its multiple antioxidative, anti-inflammatory and oncostatic actions, it could be considered as a protective agent against harmful effects of dental materials.[14-20]

CONCLUSION
Melatonin has important physiological functions that have not been yet exploited in dentistry. The various actions of melatonin mentioned herein, may have many clinical applications for improving the oral health status. With regard to etio-pathogenesis of periodontal diseases, three aspects of this condition may benefit from the use of melatonin: reducing tissue damage that is a result of free radicals, stimulating the immune response that is depressed by microorganisms in plaque, and reducing the progressive loss of alveolar bone. Melatonin is an endogen, non toxic, diffuses rapidly out of the body fluids, and penetrates all cell compartments.
Melatonin released into the oral cavity via saliva may have yet to be identified benefits for the oral health. Determination of parameters of oxidative stress in the saliva of the patients with PD could provide essential information about the susceptibility to this disease and their prognosis. Further studies need to focus their attention on the therapeutic uses of melatonin as a co-adjuvant in oral hygiene aids as and antimicrobial in local therapy to promote it as a natural inhibitor of inflammation.

REFERENCES