Zinc in Oral Health and Disease: A Narrative Review

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Zinc is an essential trace element that plays a fundamental role in maintaining oral health through its structural, catalytic, and regulatory functions. It is involved in numerous biological processes, including immune modulation, antioxidant defense, collagen synthesis, mineralization, cellular signaling, and tissue repair, all of which contribute to oral tissue homeostasis. Recent evidence has highlighted the importance of zinc homeostasis, regulated by zinc transporters and metallothioneins, in preserving normal tooth development, periodontal integrity, and wound healing. Zinc also exerts antimicrobial, anti-inflammatory, and remineralizing effects, supporting its role in the prevention and management of dental caries, periodontal diseases, and oral mucosal disorders. Furthermore, advances in biomaterials and nanotechnology have expanded the therapeutic applications of zinc through zinc-containing restorative materials, zinc oxide nanoparticles, and zinc-L-carnosine, which demonstrate promising antimicrobial, regenerative, and tissue-healing properties. Emerging evidence also suggests that salivary zinc and zinc-associated proteins may serve as potential biomarkers for oral squamous cell carcinoma, although their diagnostic and therapeutic significance remains to be fully established. Despite these promising findings, the clinical application of zinc-based interventions is limited by inconsistencies in dosage, bioavailability, and treatment protocols. This narrative review summarizes the current evidence regarding the biological functions of zinc, its role in oral diseases, therapeutic applications in dentistry, and future perspectives, highlighting zinc as a promising adjunct in maintaining oral health and improving clinical outcomes.

Keywords: zinc; oral health; oral diseases; oral cancer; tissue regeneration.

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1. Introduction

Zinc is an essential trace element that plays indispensable roles in numerous biological processes, serving as a structural, catalytic, and regulatory component of hundreds of enzymes and proteins involved in cellular metabolism, immune regulation, antioxidant defense, and tissue repair [1]. Within the oral cavity, zinc is naturally present in saliva, dental plaque, enamel, and other oral tissues, where it contributes to the maintenance of physiological homeostasis and tissue integrity [2].

Recent advances in biomaterials and nanotechnology have further expanded the applications of zinc in dentistry. Zinc-containing restorative materials, zinc oxide nanoparticles, and zinc-based oral care products have demonstrated promising antimicrobial and remineralizing properties, while zinc-containing formulations have also shown therapeutic potential for periodontal and oral mucosal diseases [3, 4]. In addition, zinc and zinc-associated proteins have emerged as potential biomarkers for oral squamous cell carcinoma, highlighting the expanding clinical significance of zinc beyond conventional nutritional supplementation [5].

Although substantial progress has been achieved in elucidating the biological functions of zinc in oral tissues, several clinical questions remain unresolved. Conflicting evidence persists regarding the efficacy of zinc supplementation in oral diseases, its influence on salivary enzymes, and its role in oral carcinogenesis [1, 6, 7]. Furthermore, uncertainty remains regarding the optimal dosage, bioavailability, and long-term safety of zinc-based interventions, while standardized clinical protocols are still lacking [8]. Therefore, this narrative review aims to summarize current evidence regarding the biological functions of zinc in oral health, its role in oral diseases, therapeutic applications in dentistry, and future perspectives for research and clinical practice.

2. Results and Discussion

Biological Functions Of Zinc In Oral Healt

Zinc is an essential trace element that supports the development, maintenance, and repair of oral tissues through its structural, catalytic, and regulatory functions. The maintenance of intracellular zinc homeostasis is tightly regulated by zinc transporters, particularly Slc39a13/ZIP13, which control zinc influx and distribution to ensure normal cellular function [9-11]. Dysregulation of these transporters has been associated with abnormalities in tooth development, connective tissue integrity, and alveolar bone homeostasis, highlighting the importance of balanced zinc metabolism in oral health [9-11].

In addition to zinc transporters, metallothioneins serve as major intracellular zinc-binding proteins that regulate zinc homeostasis while protecting cells from oxidative stress [12]. These proteins also modulate immune responses by influencing cytokine production and maintaining the balance between pro-inflammatory and anti-inflammatory signaling [12-14]. Impaired metallothionein function and zinc dysregulation have been implicated in chronic periodontal inflammation and progressive tissue destruction [14, 15].

Zinc also functions as an intracellular signaling molecule that regulates the differentiation and regenerative capacity of dental and periodontal tissues. It participates in signaling pathways, including Wnt/β-catenin and cAMP/PKA/CREB, to promote odontoblast differentiation, periodontal ligament stem cell function, and mineralized tissue formation [16-18]. These signaling mechanisms are essential for dentinogenesis, periodontal regeneration, and bone remodeling following tissue injury [16-18].

Furthermore, zinc serves as a cofactor for numerous enzymes involved in collagen synthesis, extracellular matrix remodeling, and wound healing [19]. Adequate zinc availability promotes epithelial repair and tissue regeneration, whereas zinc deficiency impairs collagen formation, delays wound healing, and increases oxidative stress [20-22]. Collectively, these biological functions establish zinc as a key regulator of oral tissue homeostasis and provide the mechanistic basis for its therapeutic application in dentistry.

Role Of Zinc In Oral Diseases

Zinc plays a protective role against several oral diseases through its antimicrobial, anti-inflammatory, antioxidant, and remineralizing properties. In dental caries, zinc contributes to reducing enamel demineralization and enhancing remineralization, particularly when combined with fluoride and calcium, although excessive zinc concentrations may inhibit crystal growth and compromise remineralization efficacy [23, 24]. Salivary zinc levels have also been investigated as indicators of caries susceptibility; however, current findings remain inconsistent across different populations [6, 25]. In addition, zinc exhibits antibacterial activity against Streptococcus mutans by disrupting bacterial membranes, inhibiting biofilm formation, and reducing acid production, thereby lowering cariogenic potential [4, 26, 27].

In periodontal diseases, zinc is involved in regulating host immune responses, inflammatory processes, and bone remodeling. Zinc deficiency impairs neutrophil function and exacerbates chronic inflammation, whereas zinc supplementation has been associated with improved periodontal healing and reduced inflammatory markers when used as an adjunct to conventional periodontal therapy [14, 28-31]. These findings highlight the importance of maintaining adequate zinc homeostasis for preserving periodontal tissue integrity and supporting periodontal regeneration.

The beneficial effects of zinc also extend to oral mucosal diseases. Owing to its anti-inflammatory and antioxidant properties, zinc has been investigated as a therapeutic agent for oral mucositis, recurrent aphthous stomatitis, and other inflammatory mucosal conditions [8, 32, 33]. Both topical and systemic zinc therapies have been reported to accelerate mucosal healing and reduce symptom severity, although additional well-designed clinical studies are still required to establish standardized treatment protocols [8].

Herapeutic Applications Of Zinc In Dentistry

The expanding understanding of zinc biology has accelerated the development of zinc-based therapeutic strategies in dentistry. As an adjunct to periodontal therapy, zinc supplementation has demonstrated beneficial effects by improving clinical periodontal parameters, reducing inflammation, and promoting tissue regeneration following scaling and root planning [30, 31, 34]. Furthermore, zinc-containing scaffolds and biodegradable biomaterials have shown considerable potential for enhancing osteogenesis and periodontal healing, although their biological performance remains highly dependent on zinc concentration and material design [35, 36].

Advances in nanotechnology have further broadened the applications of zinc in restorative dentistry. Zinc oxide nanoparticles incorporated into dental composites, adhesives, and cements enhance antimicrobial activity while promoting enamel remineralization, thereby improving the durability of restorative materials and reducing the risk of secondary caries [37, 38]. Controlled-release zinc delivery systems have also been developed to maximize therapeutic efficacy while minimizing cytotoxic effects associated with excessive zinc exposure [35, 36, 39].

Beyond restorative applications, zinc has been incorporated into oral care products and supportive therapies for oral mucosal diseases. Zinc-L-carnosine has demonstrated anti-inflammatory and antioxidant properties that accelerate healing and improve quality of life in patients with oral mucositis during cancer therapy [40-42]. Likewise, zinc-containing toothpastes and mouthwashes have been shown to modulate oral microbiota and salivary enzyme activity while reducing plaque accumulation, halitosis, and caries risk [43-45].

Zinc And Oral Cancer

Emerging evidence suggests that zinc and zinc-associated proteins are involved in the pathogenesis of oral squamous cell carcinoma (OSCC) and may serve as potential diagnostic biomarkers. Salivary zinc concentrations have been reported to decrease in patients with OSCC, indicating their potential utility as a non-invasive biomarker for early detection and disease monitoring [5, 46, 47]. In addition, several zinc-related proteins, including zinc finger protein 510 and zinc-α2-glycoprotein (ZAG), have demonstrated promising diagnostic and prognostic value, although further clinical validation is required [46, 48].

Zinc finger proteins also participate in the regulation of epithelial–mesenchymal transition (EMT), a critical process involved in tumor invasion and metastasis. Proteins such as ZEB1 have been implicated in promoting tumor progression through the regulation of EMT-related signaling pathways [49-51]. Meanwhile, ZAG has been associated with early-stage OSCC and favorable clinicopathological

characteristics, suggesting a potential tumor-suppressive role, although evidence also indicates that its overexpression may exert anti-apoptotic effects under certain conditions [48, 52, 53].

Despite these promising findings, the role of zinc in oral carcinogenesis remains complex and controversial. Current evidence indicates that zinc may exert both tumor-suppressive and tumor-promoting effects depending on the molecular context, highlighting the need for further mechanistic studies and well-designed clinical investigations before zinc can be fully integrated into precision diagnostic or therapeutic strategies for oral cancer [1, 6, 7].

3. Conclusion

Zinc plays a fundamental role in maintaining oral health through its involvement in diverse biological processes, including immune regulation, antioxidant defense, mineralization, tissue repair, and cellular signaling. These functions contribute to the preservation of oral tissue homeostasis and support the prevention and management of major oral diseases, such as dental caries, periodontal diseases, and oral mucosal disorders. Furthermore, advances in zinc-based biomaterials and nanotechnology have expanded the potential therapeutic applications of zinc in restorative and regenerative dentistry, while emerging evidence suggests its promise as a biomarker for oral cancer. Despite these encouraging findings, the clinical translation of zinc-based interventions remains limited by inconsistencies in dosage, bioavailability, and treatment protocols. Future well-designed clinical studies and mechanistic investigations are needed to establish standardized therapeutic strategies and further define the role of zinc in precision oral healthcare.

4. References

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