Zinc and Metallothionein in the Development and Progression of Dental Caries

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Abstract
Chronic oxidative stress and reactive oxygen species (ROS) in oral cavity as well as acidic pH on dental enamel surface due to the metabolic activities of bacterial plaque are the major contribution in the development and progression of dental caries. Along with other factors, deposition or dissolution Ca and Mg mostly determines the re- or demineralization of dental enamel. Zn plays an important role for both Ca and Mg bioavailability in oral cavity. Metallothionein (MT), a group of small molecular weight, cysteine-rich proteins (~7 kDa), is commonly induced by ROS, bacterial infection, and Zn. In the current review, we evaluated MT at the junction between the progression of dental caries and its etiologies that are common in MT biosynthesis.

Keywords Calcium · Magnesium · Reactive oxygen species · Metallothionein · Dental caries · Zinc

Introduction
Decay or demineralization of dental enamel also known as dental caries is a process of dissolution of apatite crystals and the net loss of calcium (Ca²⁺), magnesium (Mg²⁺), phosphate (PO₄³⁻), and other ions from the tooth surface [1]. In dental caries, the loss of Ca²⁺ mostly determines the degree of the progression of caries. Bacterial infections and oxidative stress induce the decay of dental enamel leading to caries. Cariogenic bacteria predominantly Streptococci and occasionally Lactobacilli adhere to enamel and dentin surface and produce copious amounts of acid [2–7]. Acid production in turn lowers the pH of the enamel and dentin surface below a critical level in the range of 5.2–5.5 resulting in demineralizing of the tooth structure. Again, the total antioxidant capacity (TAC) of saliva was found significantly lower in children with dental caries compared to their counterpart without dental caries [8].

Thus, development and progression of dental caries are linked with bacterial infection as well as dissolution and bioavailability of metal ions such as Ca and Mg, both of which are directly or indirectly linked with aquated zinc (Zn²⁺) in saliva. It is well known that the expression of metallothioneins (MT), a family of metal scavenging low molecular weight proteins (500 to 14,000 Da), can be induced by Zn, oxidative stress, and a variety of infectious conditions [9–16].

In the current review, we evaluated the possible involvement of MT expression (or induction) in relation to the development of carious lesions that result from the continued cariogenic bacterial metabolism in the oral cavity resulting in the dissolution of metals mainly Ca²⁺.

Zinc in Tooth Structure and Tooth Development (Dentinogenesis)
A fully erupted tooth has four major tissues: enamel, dentin, cementum, and dental pulp. Enamel consists of ~95% of minerals, mainly hydroxyapatite (HA) and ~5% of water and organic compounds. Enamel also contains proteins namely amelogenin, ameloblastin, enamelin, and tuftelin. Ninety