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# Relation of Trace Elements on Dental Health

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## Abstract

Trace elements (TEs) play an important role in human health. Toxic effects are caused by deficiency or excess of TEs. TEs have significant effects on both dental health and human health. It participates in important biological polyphosphate compound functions such as ATP, DNA, and RNA. TEs are present at different concentrations in the tooth structure. Changes in the density of some TEs affect tooth. The alteration of the density of some TEs makes the teeth more susceptible to caries. Others are protective against caries formation. Important TEs zinc (Zn), phosphorus (P), and magnesium (Mg) have important effects on dental health. Measuring the TE values through tissue sampling to identify and correct these effects has an important effect. In general, tissue samples such as blood, urine, teeth, nails, and hair are used in TE studies. Teeth are accepted as appropriate indication of TEs. As a result, TEs have significant effects on healthy tooth formation.

**Keywords:** trace elements, teeth health, human health, dental caries, dental structure

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## 1. Introduction

About 96% of life materials consist of carbon, hydrogen, and nitrogen elements. Almost 50% of the known elements are at measurable concentrations in life system. In humans and other mammals, physiological activities of 23 elements are known, 11 of which are classified as trace elements (TEs). TEs consist of transition elements [vanadium, chromium, manganese (Mn), iron (Fe), cobalt, copper (Cu), zinc (Zn), and molybdenum] and non-metal elements [selenium (Se), fluorine, and iodine]. TEs are, unlike sodium, calcium, magnesium, potassium, and chlorine, which are considered as macronutrients and required at larger amounts, fall into the micro-nutrient category, which is required at negligible levels (usually lower than 100 mg/day). Major and TEs play an essential role in human health. Lack or abundance of these elements due to natural or man-made reasons can lead to critical clinic consequences [1–4].

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A tooth consists of hard tissue (enamel, dentine, and cement) and soft tissue (pulp and periodontal ligaments), and has TE in its structure. A tooth has a multicellular structure which can cooperate functionally with maxillofacial area [5].

## 2. Enamel

Enamel is the hard tissue that covers the surface of the tooth. The function of this layer is to protect dentine-pulp complex. Enamel is the hardest and most resistant tissue in the body. It consists of 95% inorganic material (calcium hydroxyapatite crystals), 2% organic material (proteins such as amylogenic, enameline, ameloblastin, and tuftelin, among others), and 3% water [6–8]. A negligible part of the 95% inorganic material is represented by TEs. As a result of the analyses conducted using different methods in tooth enameling several chemical components are observed. These components include phosphorus (P), calcium (Ca), magnesium (Mg), zinc (Zn), lead (Pb), cobalt (Co), fluorine (F), iron (Fe), aluminum (Al), and selenium (Se). Inorganic structure of enamel consists of 36.1 Ca, 17.3 P, 3.0 carbon oxide, 0.5 Mg, 0.2 Na, 0.3 potassium (K), 0.016 F, 0.1 sulfur (S), 0.01 copper (Cu), 0.016 Zn, 0.003 silicon (Si); and low levels of silver (Ag), strontium (Sr), barium (Ba), chromium (Cr), manganese (Mn), vanadium (V), aluminum (Al), lithium (Li), and selenium (Se). TE is placed in the human tooth enamel from the environment during and after the mineralization and maturation period of the tooth [9].

## 3. Dentin

The dentin consists of 70% inorganic material (hydroxyapatite crystals and TEs), 18% organic material (type I collagen fiber and proteins such as osteonectin, osteopontin, osteoclastin-like dentin Gla protein, dentin phosphorene, dentin matrix protein, and dentin sialoprotein) and 12% water [6–8].

The inorganic material of dentin contains about 40 elements, ranging from 1000 ppm (i.e., Zn, Sr., Fe, Al, B, Ba, Pb, etc.) to 100 ppb (i.e., Ni, Li, Ag, As, Se, Nb, Hg, etc.) [10–12].

The ratio of TE in human dentin varies according to age and sex. Cobalt can be higher in women, while lead can be higher in men [13].

## 4. Cementum

Cementum is a special connective tissue that connects the periodontal ligament to the root surface, covering the outermost layer of the calcite matrix on the root surface [14].

Cement is a vascular and unlimited mineralized tissue. It is the interface between dentin and periodontal ligament and contributes to the repair and renewal of periodontal tissue after injury [15].

The inorganic component of cement is similar to bone, dentin, and enamel. The basic mineral component of the cement is hydroxyapatite with amorphous calcium phosphate ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ). The crystallinity of the cement inorganic component is lower than other calcifying tissues [16]. As a result, cement is decalcified more easily, while it has a tendency to coalesce for the adsorption of surrounding ions (i.e., fluoride). In general, the cement of adult mature teeth has higher fluoride content compared to other calcifying tissues. Mg content of the cement is about half of that in the dentin. There is a gradual increase in Mg in the deep layers of the cement [14].

## 5. Dental pulp

Tooth pulp developing from dental papilla consists of odontoblast, fibroblast, blood, and neural veins [17]. Odontoblast cells are the most important cells of the pulp. As the cells responsible for the construction of dentin and pre-dentin, they are also responsible for reparative dentin make-up in pathological cases [5, 18]. Pulp cells, especially fibroblasts, produce several inflammatory mediators such as IL-8, IL-6, and vascular endothelial growth factor in cases which threaten the health of the pulp. Tooth pulp performs a series of biological activities such as nutrition, sensitiveness, construction, and protection. The change in blood pressure and flow in the veins coming from apical region essentially affects the health of the pulp. When tooth pulp is damaged due to mechanical, chemical, thermal and microbial irritants, local tissue reactions and lymphatic, vascular inflammatory responses occur. The existence of dentin affected by oral bacteria which lead to the formation of caries is most important reasons for pulp inflammation [19].

Dental caries is a microbiological infectious disease of the teeth that results in the destruction of dental calcified tissues. There must be three factors for the formation of dental caries; bacteria (from mutans Streptococci and Lactobacillus species), susceptible tooth surface (host), and nutrient (diet) to provide bacterial growth [20, 21]. Changes in the density of TEs due to some environmental and genetic impacts have some effects on human and dental health. The change in density of some elements can lead to dental caries. Based on the previous studies on humans and animals, some classifications have been made on the impact of TE on dental caries [4, 9].

**Cariostatic elements:** Fluoride (F), Phosphorus (P).

**Mildly cariostatic:** Mo, V, Cu, Sr., B, Li, Au.

**Doubtful:** Be, Co, Mn, Sn, Zn, Br, I.

**Caries inert:** Ba, Al, Ni, Fe, Pd, Ti.

**Caries promoting:** Se, Mg, Cd, Pt, Pb, Si.

In addition, there is another classification with regard to the impact of TE on dental health:

**Cariostatic elements:** Molybdenum, Vanadium, Fluoride, Strontium, Lithium.

**Caries-promoting elements:** Selenium, Cadmium, Lead, Manganese, Copper, Zinc.

The effect on dental and oral tissues of elements and their features.

## 6. Fluoride (F)

Fluoride is an essential part of the organized matrix in hard tissues such as teeth and bones and is found in the form of fluorapatite. In addition, it can combine with calcium and stimulate osteoblastic activity. The daily recommended amount of fluoride is 0.7 mg for 1–3 ages, 1 mg for 4–8 ages, 2 mg for 9–13 ages, 3 mg for 14–18 ages, 4 mg for males above 18 years of age and 3 mg for females above 18 years of age.

Fluoride need of the body is met by drinking water, food, and tea [22].

The most well-known function of fluorine is a prevention of tooth caries. As a result of the changes created by this function dental structure, the resistance of enamel increases. In addition, it prevents the proliferation of bacteria in dental plaque. It also accelerates remineralization [4, 23].

However, during calcification of the teeth, it can lead to dental fluorosis due to excessive fluorine concentration. Dental fluorosis is a kind of enamel hypoplasia. Dental fluorosis has varying strengths from lesions in the form of white small spots on the enamel to loss of material in dental structure. The impact of excessive fluoride intake on the dental structure is a function of such factors as the fluoride concentration in drinking water, exposure amount, exposure period, and development period of the tooth [24, 25].

## 7. Vanadium (V)

Vanadium is found naturally in the soil, water, and air. Natural sources of vanadium include continental dust, sea aerosol, and volcanic emissions. The release of vanadium is associated with industrial sources such as oil refineries and power plants, especially using vanadium-rich petroleum and coal. Most foods contain naturally low vanadium concentrations. Sea products generally contain vanadium at a higher concentration than the meat of land animals. Daily vanadium uptake was reported in the range of 0.01–0.02 mg [26].

Although the role of vanadium in the development of dental caries is not clear, animal studies showed that it reduces dental caries. It is seen that when hamsters on Cariogenic diet are given vanadium, the formation of dental caries decreased. In addition, a study conducted on rats reported that when they are given intraperitoneal vanadium, the formation of dental caries reduced. On the contrary, some studies on monkeys showed that monkeys fed with water including vanadium content suffered from higher dental caries incidents [4].

## 8. Strontium (Sr)

Strontium is an element found everywhere in the environment. Stable and radioactive strontium compounds are used in many industrial processes and find applications in research and medical fields. Although strontium is not considered an important element and does not have a known biological role, it is present in all living organisms. Strontium resembles

calcium element in its properties; like calcium, it is taken up and is preferably implanted into the bone. Strontium may have both beneficial and deleterious effects on humans, depending on the amount received [27].

High strontium content is related to low caries incidence. Epidemiological studies conducted on males determined that dental caries cases involve high strontium content. One study compared good and decayed enamels and found out that strontium was higher in the good enamel. In addition, it is reported that strontium ratio in tooth decreased with aging; strontium ratio is found to be higher in young people compared to the elderly [4].

Apatites with strontium settlement are more difficult to remove from enamel compared to pure calcium component and it is stated that solution of enamel remineralized without strontium is more difficult than enamel remineralized with strontium. For this reason, it is believed that strontium adds resistance to hydroxyapatites against the solution. Strontium settlement in tooth enamel makes apatite crystal more resistant to caries due to the hetero-ionic change of calcium. The resistance of apatite crystals against demineralization which occurs as a result of acid attacks is increased [28].

## **9. Lithium (li)**

More than 90% of lithium is eliminated from the human body through the kidney. The human serum has been reported to have a lithium half-life of less than 24 hours [29].

Lithium exposure through drinking water and other environmental sources can also affect thyroid function. Lithium is used in the treatment of bipolar disorders. Lithium is found to have an indirect relationship with tooth caries. It is reported that dental caries incidence reduces in the existence of lithium. One study conducted to control the relation between lithium and dental caries determined that it reduced the dental caries incidence in humans [4]. It has also been reported the histopathologic changes in the structure of salivary glands [30].

Lithium exposure through drinking water and other environmental sources can also affect thyroid function [31].

## **10. Copper (cu)**

Copper plays an essential role in our metabolism as it is involved in the functions of several critical enzymes [28, 32].

Copper is defined as a material which increases caries. In decayed teeth, a higher level of copper is found compared to healthy teeth. Higher caries prevalence is found to be related to the existence of copper in water, food, soil or vegetables [4].

Conducted studies showed that serum copper level is significantly higher in patients with oral leukoplakia and oral submucous fibrosis and also malignant tumors such as squamous cell carcinoma [22].



Copper concentration is found to be higher compared to the enamel of healthy and primary teeth than the enamel of decayed teeth [25].

Recommended daily copper level is 340 mcg/day for 1–3 ages, 440 mcg/day for 4–8 ages, 700 mcg/day for 9–13 ages, 890 mcg/day for 14–18 ages, 900 mcg/day for males and females above 18 years of age, and 1000 mcg/day for pregnant and 1300 mcg/day for nursing women.

Copper is mostly found in oysters, sea animals with shell, whole grains, hazelnuts, potatoes, greeneries with dark leaves, dried fruits and animal products such as kidneys and livers [22].

## 11. Selenium (se)

Selenium is a vital trace element which is an essential component of antioxidant enzymes. Selenium salts are required for several cellular functions in the human body but their excessive amount is toxic [33].

Selenium is found in liver, kidneys, sea products, meat, grains, grain products, milk products, fruits, and vegetables. The recommended daily intake is 70 micrograms [22].

Selenium is a non-metallic element which is found epidemically in nature and absorbed by the body through food or inhalation. Selenium is reported to be involved in synthetic hydroxyapatite as anionic  $\text{Se}^{+4}$  through phosphate change with selenite. The ionic radius of  $\text{Se}^{+4}$  (0.50 Å) is higher than  $\text{P}^{+5}$  (Phosphate) (0.35 Å) value. For this reason, the fabric parameter increases after it is settled in synthetic hydroxyapatites [34–36].

It is found out that selenium leads to structural changes in dental dentin and mandibular condyles. Increase in dental caries emerged in the case of selenium intake. Some studies show that there is a direct relationship between caries sensitiveness and selenium ejected with urine [4].

It is reported that selenium is settled in the micro-crystal structure of the enamel at the beginning of the decay and made it more sensitive toward dissolution [25].

In addition, it is reported that decrease in selenium level in the body leads to oxidative stresses. A recent study found out that patients with oral mucositis due to a high level of chemotherapy effectively reduced the term and seriousness of oral mucositis and, in addition, sufficient selenium reinforcement can produce cytoprotective impact and antiulcer activity [22, 37].

## 12. Manganese (Mn)

Manganese content in food products varies considerably. It is highest in peanuts and grains; it is found in lowest concentration in milk products, meat, poultry, fish, and sea products. In addition, manganese can be found in coffee and tea which constitute 10% of daily intake. The body of an adult has 15 mg manganese on average which is typically seen in the nucleic acid. The daily requirement is approximately 2–5 mg/day. Manganese functions are considered as an enzyme activator and a part of metalloenzymes. Manganese is found in all mammal tissues at

concentrations varying from 0.3 to 2.9 ug manganese/g. Tissues rich in mitochondria and pigments (for example, retina, dark skin) tend to have high manganese concentrations. Bones, livers, pancreas, and kidneys typically have higher manganese concentrations than other tissues. The most important manganese store is in the bones. There are 49 elements in enamel hydroxyapatite crystals; one of them is manganese, which is usually in very slight percentages. The manganese concentrations in enamel are between 0.08 and 20 ppm, equivalent to 0.08–20 mg/kg and dentine between 0.6 and 1000 ppm. Mn concentration is at enamel-dentin limit at the external surface of enamel and higher at permanent dentition compared to primary dentition [29, 30].

Manganese is a TE which can be included in enamel through food, air, and water. In addition, Mn has the potential of changing Ca place at HAP. Several studies reported that Mn has the ability to include in synthetic HAP without degrading the crystal area size [34, 38].

Manganese is increasingly related to decay prevalence. One study found out that in areas where manganese content is higher, dental caries incidence in males increased. Therefore, it is emphasized that manganese encourages caries [4].

### 13. Zinc (Zn)

There are 2–4 grams of zinc scattered throughout the human body. Zinc is stored in the prostate, eye parts, brain, muscles, bones, kidney, and liver. It is the second most abundant transition metal in organisms after iron and is the only metal seen in all enzyme classes. In blood plasma, zinc is carried and bound to albumin (60%) and transferrin (10%). Zinc concentration in blood plasma always remains unchanged regardless of the zinc intake [22, 39, 40].

The daily average requirement of zinc is 15–20 mg/day. Approximately 2–5 mg/day is expelled through pancreas and intestines. Plasma zinc level decreases in such cases as pregnancy, loss of liquid, oral contraceptive usage, blood loss, acute myocardial infarction, infections, and malignancy [41].

Zinc plays an essential role in cell reproduction, differentiation, and metabolic activities. Zinc also supports normal growth in pregnancy, childhood, and adolescence periods [28, 42, 43]. Zinc is mostly found in animal products like meat, milk, and in fishes. Zinc bio adjustment is low in phytonutrients [22].

The role of zinc in the development of dental caries is controversial. One study which analyzed the existence of TEs in children found zinc levels of children with more dental caries to be higher. In addition, it has been found out that zinc concentration in caries enamel of milk teeth was higher. However, another study showed that existence of zinc in saliva decreased the development of dental caries [4, 44, 45].

Contrary to the foregoing, zinc is added to oral health products in order to control plaques, reduce halitosis and delay tartar development. The zinc released from mouthwash solutions and toothpastes can continue to exist in plaque and saliva for a long time. Low zinc concentrations can reduce enamel remineralization. However, their anticariogenic impact is still controversial. Zinc deficiency is reported to be a potential risk factor for oral and



periodontal patients. Parakeratotic changes in cheeks, tongue, and esophagus are indicators of zinc deficiency. Serum zinc level has been found to be at lower levels in patients with potentially premalignant disorders such as oral leukoplakia [22, 43, 46].

## 14. Cadmium (Cd)

Cadmium is found in some vegetables (leaved vegetables, potatoes, grains, and seeds) and animal food (liver and kidney). The moment cadmium enters the body, it accumulates in the liver and bones and is expelled very slowly (cadmium reference). Cadmium is an active element in soil and can be received by plants easily. As a result of being received by plants and entering the food chain or possibility of reaching water environment by being washed from the soil, it creates a significant environmental problem. In addition, the downward carriage of cadmium from the soil with chelating agents accelerates and it can lead to pollution in drinking and irrigation waters as it enters underground water sources [47, 48]. Exposure to cadmium is related to some various systematic health impacts such as kidney failure, skeleton disorders, and cardiovascular diseases [49]. Cadmium can be released from intraoral alloys in dentistry patients and accumulate in teeth and mouth tissues, which are strictly bound to metallothioneins [50]. The relation has been found between cadmium and the increase in decay prevalence. However, it is stated that settlement of cadmium in teeth after growth is not effective on caries. Some studies conducted on test animals indicate that there is a strong relationship between the formation of dental caries and cadmium intake in dental development period [4]. The increase of exposure to and dispersion of this toxic material is becoming increasingly important on the systematic and oral health of sensitive populations such as children [49].

## 15. Lead (Pb)

People can be exposed to lead through contaminated food and beverage, resulting from industrial activity [51]. Lead is added to the food chain especially through vegetables growing on contaminated soil. Lead can be transferred with plants and grass from contaminated soil, which potentially leads to the accumulation of toxic metals in vegetating ruminants and especially in cattle. The accumulation of lead creates toxic effects in cattle; it also leads to toxic effects in people who consume meat and milk contaminated with toxic metals [52].

It is a harmful and toxic metal for the human body. Lead has the ability to translocation with  $\text{Ca}^{+2}$  at the HAP of teeth. For this reason, it downsizes the HAP crystals [34, 53].

Lead is transferred to the tissues of the body such as teeth through environment or nutrition. It is determined to have an encouraging effect on dental caries. In addition, it is found out that lead increases the formation of enamel hypoplasia. A positive correlation has been found between saliva lead levels and decay development of children with early childhood decays. Thus, lead plays an essential role in the development of new caries lesions [4, 53, 54].

## 16. Iron (Fe)

Unlike other TE, iron (Fe) is abundant in nature and a biologically essential component of every living organism. Nevertheless, despite geological abundance, when oxygen contacts iron, hardly soluble oxides are created. For this reason, it is not easily received by organisms [55].

These are most common dietary resources for iron: liver, meat, poultry products and fish; cereals, green leafy vegetables, pulses, nuts, oilseeds, and dried fruits [22].

As an essential element, iron mostly enters the body with green vegetables. It is reported that iron concentrations are low in enamel [34].

The amount of Fe is 4–5 gm in healthy individuals. Iron (Fe) is a trace metal that is necessary to ensure that almost all organisms survive. Participation in heme and iron–sulfur cluster containing proteins allows Fe to participate in a variety of vital functions such as oxygen transport, DNA synthesis, metabolic energy, and cellular respiration [56].

Some studies reported that iron can act as preventive for dental caries. The study reported that adding 2 mmol/L  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$  to acidic drinks reduced mineral loss and human enamel preserved the surface microhardness [57, 58].

In addition, some iron addition products used for iron deficiency anemia are reported to have a cariostatic effect and delayed the emergence of dental caries in human teeth. As a result of iron deficiency, angular cheilitis, atrophic glossitis, diffused oral mucosal atrophy, candidal infections, oral premalignant lesions, and stomatitis can be seen in the oral region [22].

Besides all these explanations, some factors change the density of the TEs on the teeth such as exposure to electromagnetic fields, Wi-Fi, radio frequencies emitted from mobile phones, environmental pollution, excessive fertilization of soil, natural disasters, and dental anomalies [3, 27, 49, 50].

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