



Zinc and Oral Health: Literature Review

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Abstract

Introduction: Zinc was a trace element of great importance in the oral cavity. It was naturally present in various places such as dental plaque, dental hard tissues and saliva. **Main Goal:** our work was to highlight the importance of zinc in maintaining optimal oral health. **Materials and Methods:** The research was carried out with computerized databases Pubmed, ScienceDirect, and Google scholar and manual search from previously identified references. Relevant articles were identified after reading their titles, abstracts or reading the entire document. **Results:** 19 articles were retained after eliminating articles that did not meet our objectives or had irrelevant content. **Discussion:** Zinc was of great importance in dental protection during the demineralization process and was used in the prevention and treatment of various oral pathologies. It had antibacterial effects allowing it to control the formation of plaque. In mouthwashes and toothpastes, zinc salts were part of several compositions leading to different effects, including the neutralization of bad breath, antiseptic and anti-inflammatory effects. **Conclusion:** Zinc has been shown to be effective against common oral health problems such as tooth decay, gingivitis, periodontitis and unpleasant odours. However, further research studies are required to determine the effect of zinc supplementation in the treatment of oral diseases.

Subject Areas

Dentistry

Keywords

Zinc, Oral Health, Hydroxyapatite, Gingivitis, Dental Plaque

1. Introduction

Zinc (Zn), a metal from the earth's crust, constitutes the most abundant trace element in the human body after iron and it has been found in all tissues and all body secretions with relatively high concentrations. In the oral cavity, zinc has been found in saliva, dental plaque and dental hard tissues and contributes to healthy tooth formation. Thanks to its antibacterial, healing and anti-inflammatory properties, zinc has been used in mouthwashes and toothpastes and induced in dental biomaterials and orthodontic materials for its immune and preventive properties against the formation of dental plaque. The objectives of our work were to take stock of the importance of zinc in maintaining optimal oral health and were represented in the study of the possible effects of zinc on caries and dental plaque, the determination of possible effects of adding zinc to toothpastes and mouthwashes and highlighting the relationship between zinc and oral pathologies.

2. Materials and Methods

The search was carried out following two types of strategies, where we admitted articles meeting the objectives of our research published during the last 10 years in English, and we eliminated everything that was not included in this selection.

2.1. Digital Research Strategy

Initially, the research was carried out on computer databases accessible via the Internet then we looked for published data by searching several bibliographic databases. By querying the computerized databases Pubmed, Medline, EBSCO, ScienceDirect, and Google scholar, using the keywords (zinc, oral health, mouth diseases, gingivitis, dental plaque, hydroxyapatite, dental enamel) using CISMef (catalogue and index of French-language medical sites) to facilitate the search. The electronic search was supplemented by a manual search using bibliographies of selected articles.

Boolean equations:

- Zinc AND Oral health
- Zinc AND Mouth disease
- Zinc AND Gingivitis
- Zinc AND Dental plate
- Zinc AND Hydroxyapatite
- Zinc AND Mouth disease AND Dental plaque

Below is the electronic search history:

In the last 10 years the number of published articles about:

- Zinc: 68898, Oral Health: 8928, Mouth Diseases: 86122, Gingivitis: 20380, Dental Plaque: 8695, Hydroxyapatite: 7150, Dental enamel: 5049
- Zinc AND Oral health: 2, Zinc AND Mouth diseases: 61, Zinc AND gingivitis: 6, Zinc AND Dental plaque: 10, Zinc AND Hydroxyapatite: 88, Zinc

AND Dental enamel: 22, Zinc AND Mouth disease AND Dental plaque: 4

2.2. So-Called Bottom-up-Manual-Search Strategy

This search strategy gave us the chance to further collect a number of articles from the reference list of already pre-selected articles, which would have escaped the electronic search of interest to our subject.

2.3. Inclusion Criteria

During our bibliographic search, we included articles that met the objectives of our research, published during the last 10 years, *i.e.* from 2011 to 2021 and articles published in English.

2.4. Exclusion Criteria

We eliminated articles that did not meet our research objectives, published before 2011, and published in a language other than English.

3. Results

3.1. Selection of Articles

The selected articles were subject to a critical methodical reading, to retain only those articles of sufficient methodological quality (**Figure 1**).

The initial search yielded 758 articles based on the Boolean equations mentioned in (**Table 1**). We kept 19 articles that met our reliability criteria and addressed the heart of our subject.

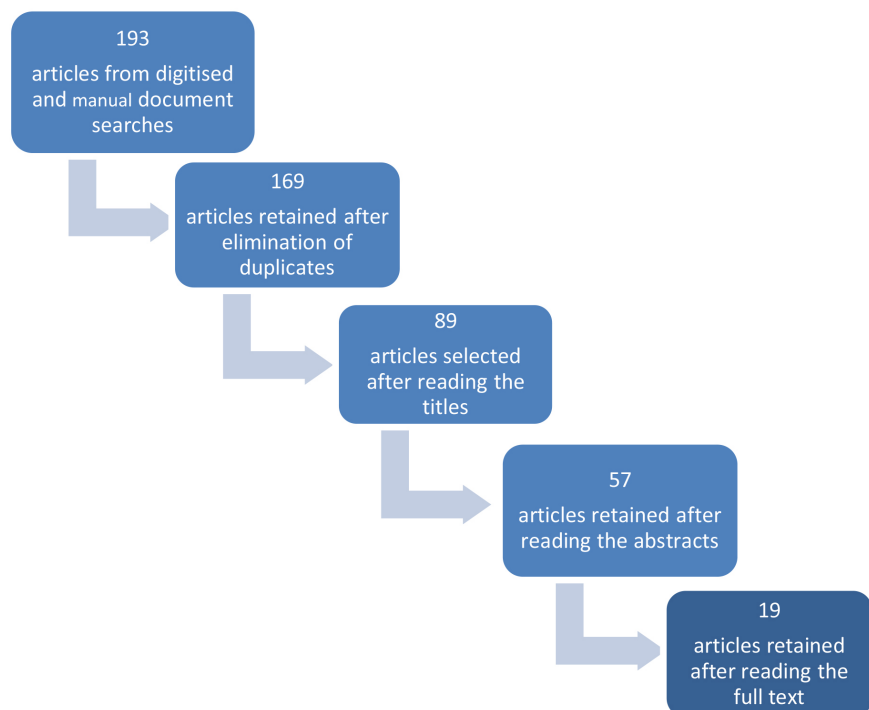


Figure 1. Search flowchart and article selection.

Table 1. Summary table of selected articles.

N°	Article title	Authors	Year	Bibliographic reference
1	A Randomized Clinical Study to Examine the Oral Hygiene Efficacy of a Novel Herbal Toothpaste with Zinc over a 6-Month Period	Nandlal B. <i>et al.</i>	2021	14
2	Recent Development of Active Ingredients in Mouthwashes and Toothpastes for Periodontal Diseases	Rajendiran M. <i>et al.</i>	2021	17
3	Reductions in Clinical Inflammation and Oral Neutrophils with Improving Oral Hygiene	Prasad K.V.V <i>et al.</i>	2020	15
4	Comparative Fluoride Release and Antimicrobial Analysis of Commercial and Experimental Bioactive Glass/Nano-Oxide-Based Dentifrices	Gul H. <i>et al.</i>	2020	12
5	Zinc Adequacy Is Essential for the Maintenance of Optimal Oral Health	Uwitonze A. <i>et al.</i>	2020	16
6	Zinc Therapy in Treatment of Symptomatic Oral Lichen Planus	Kandi P. <i>et al.</i>	2019	18
7	Zinc and Metallothionein in the Development and Progression of Dental Caries	Rahman M.T. <i>et al.</i>	2019	1
8	Inhibitory Effect of Zinc-Containing Desensitizer on Bacterial Biofilm Formation and Root Dentin Demineralization	Nikaido T. <i>et al.</i>	2019	6
9	The Effects of Two New Dual Zinc plus Arginine Dentifrices in Reducing Oral Bacteria in Multiple Locations in the Mouth:12-Hour Whole Mouth Antibacterial Protection for Whole Mouth Health	Prasad K. <i>et al.</i>	2018	13
10	Improvement of Dysgeusia by Polaprezine, a Zinc-L-Carnosine, in Outpatients Receiving Cancer Chemotherapy	Fujii H. <i>et al.</i>	2018	19
11	Antimicrobial Efficacy of Mouthwashes Containing Zinc-Substituted—Nanohydroxyapatite and Zinc L-Pyrrolidone Carboxylate on Suture Threads after Surgical Procedures	Cosola S. <i>et al.</i>	2017	8
12	A Comparison of the Effect of Triamcinolone Ointment and Mouthwash with or without Zinc on the Healing Process of Aphthous Stomatitis Lesions	Mehdipour M. <i>et al.</i>	2016	10
13	Zinc: A Precious Trace Element for Oral Health Care?	Tayyaba F. <i>et al.</i>	2016	4
14	Antimicrobial Effectiveness of Cetylpyridinium Chloride and Zinc Chloride-Containing Mouth Rinses on Bacteria of Halitosis and Peri-Implant Disease	Kang J.H. <i>et al.</i>	2015	7
15	Polaprezine Reduces the Severity of Radiation-Induced Mucositis in Head and Neck Cancer Patients	Doi. H <i>et al.</i>	2015	9
16	Physical Chemical Effects of Zinc on in Vitro Enamel Demineralization	Mncimne M. <i>et al.</i>	2014	3
17	Zinc Induces Apatite and Scholzite Formation during Dentin Remineralization	Osorio R. <i>et al.</i>	2014	5
18	Zinc in the Mouth, Its Interactions with Dental Enamel and Possible Effects on Caries; a Review of the Literature	Lynch RJM	2011	1
19	Antimicrobial Effects of o-Cymen-S-ol and Zinc, Alone & in Combination in Simple Solutions and Toothpaste Formulations	Pizzey RL. <i>et al.</i>	2011	11

3.2. Potential Effects of Zinc on Demineralization/Remineralization

According to the World Health Organisation (WHO), dental caries is a pathological process localised in the enamel and/or dentin, caused by the formation of acids from the fermentation of carbohydrates by bacteria in the mouth. Resulting in the dissolution of apatite crystals and a net loss of calcium (Ca^{2+}), magnesium (Mg^{2+}), phosphate (PO_4^-) and other ions from the tooth surface, such as zinc [1].

The appearance of caries is affected—among other things—by the quantitative and qualitative characteristics of the oral bacterial flora, as well as by the quantity of microelements present in saliva, which, in its physiological state, maintains moisture in the oral cavity with a high self-cleaning capacity, as well as stabilising and preserving the bacterial flora [1].

3.2.1. Zinc and Dental Enamel

Zinc has long been associated with a reduction in the solubility (demineralisation) of enamel and can modify the crystal growth of calcium phosphates involved in remineralisation, as it acts on enamel surfaces at PO_4^{3-} sites in the hydroxyapatite network—eventually forming an a-hopeite phase, whose formula is a $-\text{Zn}_3(\text{PO}_4)_2 \cdot 4\text{H}_2\text{O}$. According to studies in an acidic environment, zinc reduces the solubility of enamel by acting as an inhibitor of matrix metalloproteinases (MMPs), stimulating a metabolic effect in the mineralisation and remineralisation processes of hard tissue and influencing signalling pathways. Low concentrations of zinc can inhibit remineralisation, as well as significantly reduce enamel dissolution [2] [3].

Studies with synthetic hydroxyapatite have shown that zinc is easily acquired by apatite, because it competes with calcium and then protects the enamel from carious damage [4].

3.2.2. Zinc and Dentin

Studies have shown that storing dentin in zinc-containing solutions maintains its remineralisation. During this process, a complex of calcium phosphate and hydrated zinc is formed, which has anti-inflammatory and antibacterial effects, as well as osteoconductivity. This has the potential to repair dentin and achieve a balance between the processes of demineralisation and remineralisation of dentin [5].

Zinc also influences signalling pathways. It plays an important role in the closure of dentinal tubules and the formation of mineral tags. It also inhibits the formation of biofilm on root dentin by blocking bacterial growth and plays a role in resistance to demineralisation by reducing mineral loss [6].

3.3. Potential Effects of Zinc on Dental Plaque

Zinc is an effective antioxidant that reduces the production of toxic agents such as hydrogen peroxide (H_2O_2), which has harmful effects on host cells. Numerous

in vivo and in vitro studies have shown that zinc has the ability to inhibit and limit the production of acids in dental plaque. More specifically, under normal saliva pH, zinc reduces acid production by *Streptococcus mutans*, one of the most cariogenic bacteria [4].

3.4. The Role of Zinc in Dental Prescriptions

3.4.1. Use of Zinc in Mouthwashes

Mouthwashes sometimes contain zinc chloride, which, at a minimum concentration of 0.2%, has been shown to inhibit tartar and act as an antibacterial agent [2].

- **Mouthwashes that neutralise bad breath:**

Contain both antiseptics to limit bacterial growth and agents that neutralise the volatile sulphur compounds responsible for bad breath. This category includes mouthwashes based on zinc chloride with cetylpyridinium chloride [7].

- **Antiseptic mouthwashes designed to control plaque formation and improve gingival condition:**

By inhibiting bacterial growth generally contain zinc-substituted nanohydroxyapatite and L-pyrrolidone zinc carboxylate that provides the same antibacterial efficacy as mouthwash containing chlorhexidine, but without causing tooth discolouration or taste alterations, which are typical side effects of chlorhexidine [8].

- **Anti-inflammatory mouthwashes:**

Zinc-L-carnosine mouthwashes, which have been shown to have a positive effect on reducing the incidence of oral mucositis and its symptoms. Mouthwashes based on zinc and triameinolone, which appear to be just as effective in the wound-healing process as in the typical treatment of recurrent aphthous stomatitis [9] [10].

3.4.2. Use of Zinc in Toothpastes

• **In toothpastes containing zinc with o-cymen-5-ol:**

Zinc chloride is the main salt used for its described effects on the gingival state, in particular inhibition of the bacteria *Streptococcus mutans*, *Escherichia coli*, *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, as well as reducing the incidence of gingivitis and periodontitis. Following the same principle, zinc oxide is added to fluoride-doped bioactive glass-based toothpastes for its effects on caries, which treats early white spots and controls plaque [11] [12].

• **In toothpastes containing fluoride and L-arginine:**

Zinc citrates or zinc oxides are added to provide 12-hour antibacterial protection for the whole mouth (tongue, cheeks, gums, teeth and saliva). The main effect of fluoride and plant-based ingredients (*Syzygium Aromaticum*, *Embllica Officinalis*, *Aloe Barbadosensis*, *Azadirachta Indica*, *Ocimum Basillicum* and *Apis Mellifera*) containing toothpastes is to reduce bad breath through bacterial inhibition, as well as inhibiting the formation of dental plaque and improving gingival condition [13] [14].

3.5. Zinc and Oral Diseases

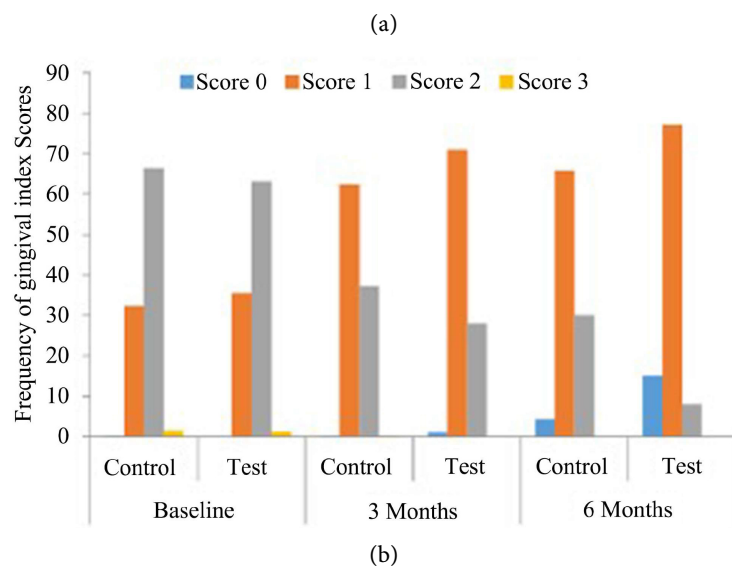
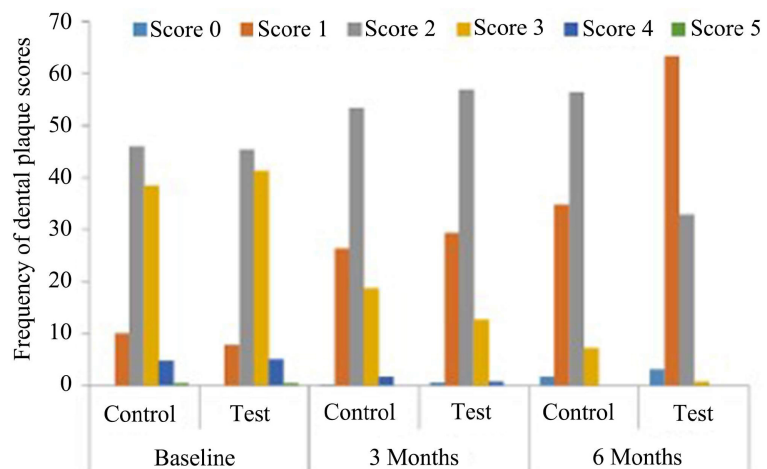
3.5.1. Zinc and Periodontal Pathologies

1) Zinc and gingivitis

In a state of gingival inflammation, neutrophils (PNN) are the most abundant leucocyte population in inflammatory states of the mouth. Reducing their numbers in an oral environment means reducing inflammation and the establishment of optimal oral hygiene [15].

Zinc is retained in plaque and saliva for many hours after application. It can combat the *Fusobacterium nucleatum* and *Prevotella intermedia* responsible for gingivitis, as well as inhibiting the proteases produced by *Porphyromonas gingivalis* [11].

Several studies have demonstrated the positive effect of toothpastes containing zinc on improving oral hygiene. The reduction in the plaque index, the gingival index, and a reduction in the number of neutrophils after regular use of these toothpastes indicate an improvement in gingival condition through significant reductions in inflammation and bleeding, as well as improved plaque control (Figure 2) [14] [16].



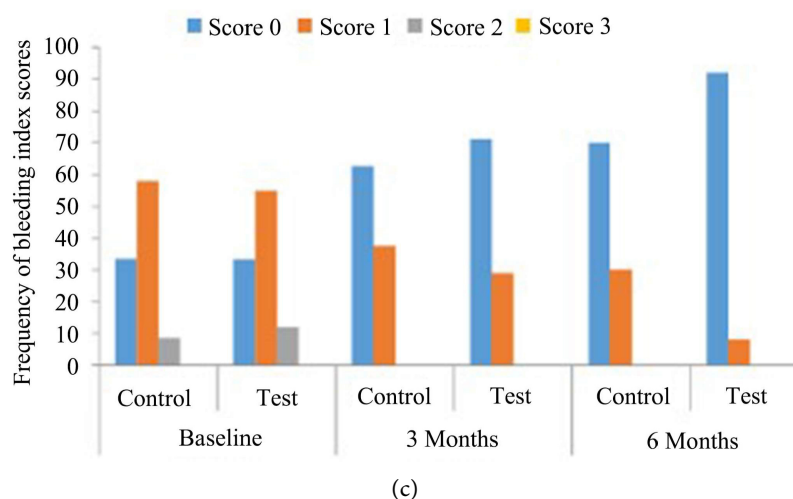


Figure 2. Zinc and improved gingival condition [14]. (a): Frequency distribution of dental plaque scores over 6 months of zinc use. (b): Frequency distribution of gingival index scores over 6 months of zinc. (c): Frequency distribution of gingival bleeding index scores over 6 months of zinc use.

2) Zinc and periodontitis

Gingivitis can progress to periodontitis, which is the irreversible destruction of the underlying connective tissue and alveolar bone as a result of plaque build-up. Zinc is capable of eliminating the bacteria *Streptococcus mutans*, *Streptococcus aureus*, *Streptococcus salivarius*, *Streptococcus sobrinus*, *Lactobacillus casei*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Treponema denticola* and *Tanarella forsythia* found in the different types of periodontal disease [17].

Periodontitis can therefore be prevented and reversed by oral hygiene methods that eliminate the build-up of plaque that effectively eliminate plaque biofilm. The inclusion of zinc in the composition of mouthwashes and toothpastes, has bactericidal and bacteriostatic effects, as well as protecting against periodontitis [11] [17].

3.5.2. Zinc and Recurrent Aphthous Stomatitis

Recurrent aphthous stomatitis is characterised by recurrent, round, shallow oral ulcers surrounded by inflammation, primarily involving the non-keratinised mucosa. Zinc is effective in reducing recurrence rates in recurrent aphthous stomatitis. Zinc therapy for recurrent aphthous stomatitis was recommended as aphthous ulcers were reduced in size following treatment. Zinc mouthwashes therefore appear to be effective in the management and prevention of this condition [10].

3.5.3. Zinc and Oral Lichen Planus

Oral lichen planus is an autoimmune, inflammatory disease in which auto-cytotoxic T lymphocytes (CD8+ cells) trigger apoptosis of basal cells of the oral epithelium by recognising major histocompatibility complex (MHC)-I associated

antigen on keratinocytes. Activated CD4+ lymphocytes increase the number of Langerhans cells and up-regulate MHC-II expression, leading to improved recognition of the antigen recognition. Activated T lymphocytes release cytokines that damage basal keratinocytes via tumour necrosis factor (TNF)- α and granzyme B, leading to keratinocyte apoptosis. Through the disrupted epithelium, cytokines attract additional lymphocytes into the developing lesion. Case reports have noted that in cases of zinc deficiency, the lymphocyte reaction is inhibited, which results in the disturbance of the development and function of T lymphocytes that leads to a reduction in their numbers [18].

3.5.4. Use of Zinc in Treatment of Halitosis

Zinc chlorides effectively inhibit the bacterial growth responsible for halitosis, particularly bacteria such as *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Treponema denticola*, and *Staphylococcus aureus*. However, to improve the effectiveness of halitosis treatment, the selection of approaches must be individualized based on the verification of the patient's intra-oral bacterial composition. Personalized mouthwashes with different combinations of therapeutic agents, could be a solution to overcome the limitations of effectiveness with fixed composition agents [7].

3.5.5. Zinc and Oral Malignancy and Risk

It has been suggested that zinc is of key importance in the treatment of immunocompromised individuals suffering from oral diseases, particularly those undergoing chemotherapy or radiotherapy. Zinc exhibits anti-inflammatory activities and is a component in many DNA repair proteins. It plays an important role in the production of the protein metallothionein, which protects against oxidative cell damage [4] [16].

Studies suggested that zinc ions serve as tumor markers since their increase encourages survival of immune cells and elimination of tumor cells. They showed that excess zinc causes copper deficiency, and Low serum copper also appears to be linked to oral cancer risk [4] [16].

3.5.6. Treatment of Chemotherapy-Related Dysgeusia

As for dysgeusia linked to chemotherapy, it is defined as an alteration of taste present in patients undergoing chemotherapy in different forms up to ageusia.

The use of the compound zinc-L-carnosine or polaprezine significantly reduces the duration of dysgeusia. Likewise, the administration of fluoropyrimidines, which inhibit the absorption of zinc in the human body and promote its chelation, in patients undergoing chemotherapy appears to increase the risk of dysgeusia, therefore establishing a clear relationship between zinc and dysgeusia linked to chemotherapy [19].

3.5.7. Oral Mucositis Induced by Radiotherapy

Oral mucositis is an acute inflammation of the oral mucosa following exposure to chemotherapy or radiotherapy. It harms the quality of life of patients. They

suffer from mouth pain causing them difficulty eating, drinking and swallowing.

Recent studies have determined that the use of Polaprezinc partially prevents and decreases the incidence of mucositis in head and neck cancer patients undergoing radiation therapy. It helps relieve symptoms related to this affection. The authors concluded that zinc is a promising strategy to delay the onset of radiotherapy-induced oral mucositis and reduce its intensity [9] [16].

4. Discussion

4.1. General Information on Zinc

- Zinc is present in several foods. The richest sources would be red meats and shellfish. The bioavailability of zinc from animal sources is relatively high since it presents compounds that inhibit the absorption of zinc. The recommended daily ratio amounts of zinc are numbers estimated to be necessary to prevent individuals from manifesting symptoms of deficiency or toxicity [20].

The reference nutritional intake is presented in (Table 2) by age group and gender.

Table 2. Nutritional reference intake of zinc by age and gender [20].

Age	Estimated average need (mg/d)		Recommended nutritional intake (mg/d)		Tolerable upper intake level (mg/d)
	Males	Females	Males	Females	
0 - 6 months	-	-	-	-	4
7 - 12 months	2.5	2.5	3	3	5
1 - 3 years old	2.5	2.5	3	3	7
4 - 8 years old	4	4	5	5	12
9 - 13 years old	7	7	8	8	23
14 - 18 years old	8.5	7.3	11	9	34
≥19 years old	9.4	6.8	11	8	40
Pregnant woman ≤18 years old	-	10	-	12	34
Pregnant woman 19 - 50 years old	-	9.5	-	11	40
Breastfeeding woman ≤18 years old	-	10.9	-	13	34
Breastfeeding woman 19 - 50 years old	-	10.4	-	12	40

-: no value associated. Mg/d: milligrams per day.

- There is a delicate **homeostatic control** of zinc at the cellular level that prevents excessive zinc accumulation. It is mediated by at least 10 zinc transporters (ZnT) and 15 zinc importers (Zip). ZnT allows the export of zinc from the cell cytoplasm, while Zip ensures the influx of zinc into the cytosol from the extracellular space and the intracellular lumen towards the cytoplasm. Another way of maintaining intracellular zinc homeostasis is to use metallothioneins, zinc-binding proteins, which can act to buffer cellular zinc [21] [22].
- **Zinc loss** through the gastrointestinal tract accounts for about half of all zinc eliminated from the body. Other routes of zinc excretion include urinary losses and superficial losses from flaky skin, hair or sweat [16] [21] [22].
- **At the cellular level**, zinc plays a number of roles: catalytic, structural and regulatory. Zinc-dependent enzymes control DNA synthesis, normal growth, behavioural response, brain development, reproduction, foetal development, membrane stability, bone formation and wound healing. Zinc is essential for the function of a number of metalloproteins and regulates both enzyme activity and protein stability as an activator or inhibitory ion [21].
- **Zinc presents a toxicity**, which is reduced since its regulation takes place in several absorption sites as well as in the excretion sites [20].
- **COVID-19** or coronavirus disease 2019 is a condition caused by a virus of the Coronaviridae family, SARS-CoV-2. This disease was initially reported to affect the respiratory, gastrointestinal and neurological systems. The oral, olfactory and integumentary systems are also involved [23]. Existing data support the hypothesis that zinc supplementation during the pandemic would be a safe, inexpensive, and adjunctive treatment to reduce the risk of infection and severe disease progression. Procedures to reduce viral load in the oral cavity are therefore important [24] [25]. A randomised pilot clinical trial demonstrated that the use of a zinc and cetylpyridinium chloride mouthwash significantly reduced the SARS-CoV-2 viral load in saliva for up to 60 minutes after rinsing [25].

4.2. Summary of Results

In view of the above, we have noted that the analysis carried out on the subject of zinc reveals several satisfactory results such as, for example, the positive effects of zinc on dental plaque and on the reduction of the incidence of caries (see **Tables 3-5** and **Figure 3**).

Table 3. Effects of zinc on enamel, dentin, caries incidence and dental plaque.

	Effects of zinc	Reference
	Reduction of enamel solubility (demineralisation) by:	
Enamel	- Inhibiting matrix metalloproteinases.	[1]-[4]
	- Forming a poorly soluble a-hopeite phase resistant to acid conditions.	

Continued

	<ul style="list-style-type: none"> - Competing with calcium and reaching a position on the apatite crystal. <p>⇒ Protection of the enamel from carious damage.</p>	
	<ul style="list-style-type: none"> - Influence on signalling pathways stimulating a metabolic effect in dentin mineralisation processes. - Closure of dentinal tubules and formation of mineral tags. 	
Dentin	<ul style="list-style-type: none"> - Inhibition of biofilm formation on root dentin. - Formation of calcium and zinc phosphate hydrate complex. <p>⇒ Potential for dentin repair and remineralisation.</p> <p>⇒ Resistance to demineralisation.</p>	[5] [6]
	<ul style="list-style-type: none"> - Antioxidant effect reducing the production of toxic agents. - Disrupts the respiration of <i>Fusobacterium nucleatum</i> bacteria and other buccal microflora. 	
Dental Plaque	<ul style="list-style-type: none"> - Stops the production of reactive oxygen. - Inhibition of exopolysaccharide production by glucosyl-transferases in bacteria. <p>⇒ Inhibits the production of acids in dental plaque.</p>	[4]

Table 4. Toothpastes and zinc.

Toothpaste composition	Zinc salts used	Effects	References
		Effects on gingival condition	
Zinc and o-cymen-5-ol	Zinc chloride	<ul style="list-style-type: none"> - Antibacterial effect (<i>Streptococcus mutans</i>, <i>Escherichia coli</i>, <i>Porphyromonas gingivalis</i>, <i>Fusobacterium nucleatum</i>) - Anti-periodontitis effect - Anti-gingivitis effect 	[11]
		Effects on caries	
Zinc and bioactive nano glass doped with fluoride	Zinc oxide	<ul style="list-style-type: none"> - Release of fluoride - Antibacterial effect (<i>Streptococcus mutans</i>, <i>Lactobacillus casei</i>) - Treatment of early white spots - Plaque control 	[12]
fluorine and L-arginine and Zinc	Zinc oxide Zinc citrate	<ul style="list-style-type: none"> - 12-hour antibacterial protection for the entire mouth (tongue, cheeks, gums, teeth and saliva) 	[13]
Zinc, fluoride and plant-based herbal ingredients: <i>Syzygium Aromaticum</i> , <i>Emblica Officinalis</i> , <i>Aloe Barbadensis</i> , <i>Azadirachta Indica</i> , <i>Ocimum Basillicum</i> and <i>Apis Mellifera</i>	Zinc citrate Zinc chloride	<ul style="list-style-type: none"> - Anti-halitosis effect - Antibacterial effect - Inhibits plaque formation - Improves gingival condition by reducing gingival index and bleeding 	[14]

Table 5. Zinc and oral pathologies.

Pathologies	Zinc effects	References
Gingivitis	<ul style="list-style-type: none"> - Anti-bacterial effect against the bacteria responsible for gingivitis - Reduces plaque index - Reduced neutrophil count - Reduced inflammation and bleeding - Reduced gingival index - Better control of dental plaque ⇒ Improved gingival condition 	[11] [14]-[16]
Periodontitis	<ul style="list-style-type: none"> - Bacteriostatic effects - Bactericidal effect on: Streptococcus mutans, Streptococcus aureus, Streptococcus salivarius, Streptococcus sobrinus, Lactobacillus casei, Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Treponema denticola and Tannerella forsythia ⇒ Prevention and treatment of periodontitis 	[11] [17]
Recurrent aphthous stomatitis	<ul style="list-style-type: none"> - Reducing the size of lesions following treatment with zinc - Use of zinc in the management and prevention of the disease 	[10] [16]
Oral lichen planus	<ul style="list-style-type: none"> - Prevents disruption of the development and function of T lymphocytes - Maintains the physiological number of T lymphocytes - Role in lymphocyte division, maturation and differentiation ⇒ Healing effect of zinc therapy ⇒ Reduced burning sensation 	[18]
Oral cancer	<ul style="list-style-type: none"> - Survival of immune cells - Elimination of tumour cells - Use of zinc ions as tumour markers 	[4] [16]
Dysgeusia	<ul style="list-style-type: none"> - Use of zinc inhibitors appears to increase the risk of dysgeusia - Reduction in median recovery time and symptoms following zinc therapy 	[4] [16]
Oral mucositis	<p>Controversial results:</p> <ul style="list-style-type: none"> 1) Zinc sulphates - No effect on oral mucositis 	[9] [16]

Continued

2) Polaprezinc

- Relief of symptoms
- Reduces the intensity of oral mucositis
- Prevention and reduction in the incidence of the condition

- Inhibition of bacteria that produce volatile sulphur compounds:

Halitosis Fusobacterium nucleatum, Porphyromonas gingivalis, Treponema denticola, Staphylococcus aureus, Aggregatibacter actinomycetemcomitans, Prevotella intermedia and Tannerella forsythia [7]

⇒ Reduction of unpleasant mouth odours

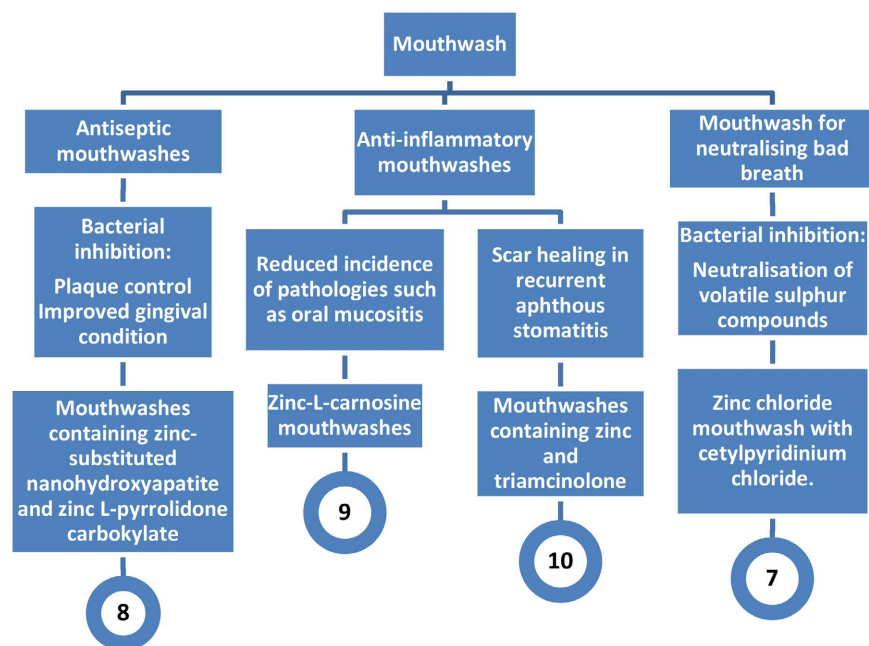


Figure 3. Different mouthwashes containing zinc.

4.3. Zinc and Oral Cavity

4.3.1. Effects of Zinc on Dental Plaque and Tartar Formation

- The action of zinc in reducing plaque growth occurs when zinc binds to the oral bacterial surface and modifies its surface potential to reduce bacterial adhesion to teeth [26].
- Zinc may also inhibit bacterial acid production in plaque by altering the metabolic activity of oral bacteria, thereby reducing bacterial growth [27].
- These effects, in synergy with the reported effect of zinc on reducing microbial growth and plaque formation, make zinc an effective anti-scale agent [28].

4.3.2. Zinc and Dental Demineralization

- Zinc binds to lipoteichoic acid associated with plaque bacteria in biofilms in a similar manner to calcium. This mechanism may increase the concentration of zinc ions in oral fluids to protect dental tissues from further demineralization [29].
- In 2000, it was reported that the dissolution rates of zinc-containing synthetic carbonated hydroxyapatite were significantly lower than with no zinc in the apatite structure. In vitro and in situ studies have revealed that zinc oxide can have a significant effect on inhibiting dentin demineralization [30] [31].
- We then note that the effects of zinc as an anti-plaque and anti-tartar agent were widely studied before the year 2011. The interaction of zinc with dental tissues and its role in demineralization and remineralization were considerably less well understood.

4.3.3. Zinc Toothpastes and Mouthwashes

- Toothpastes containing zinc citrates alone significantly reduce the formation of supragingival plaque and gingivitis. They inhibit the production of oral streptococci and reduce oral anaerobic microflora [32] [33].
- Concerning toothpastes containing zinc citrates in combination with triclosan and toothpastes based on fluoride and zinc, an antibacterial effect has been noted. These toothpastes can lead to a buildup of antibacterial agents in plaque, which continue to work even after dietary intake [27] [34] [35].
- Toothpastes containing zinc citrates, bromochlorophene and triglyceride can inhibit gingival inflammation by inhibiting the formation of dental plaque. Combining zinc with triclosan has demonstrated effects on reducing plaque and gingivitis [36] [37].
- Mouthwashes containing zinc chloride and essential oils have demonstrated effects in reducing tartar in people with moderate rates of this formation. While combination of zinc and chlorhexidine even if low concentrations effective in eliminating volatile sulfur compounds that cause bad breath [38] [39].
- We note that in articles from 2011 to 2021, a large amount of toothpastes and mouthwashes were studied. Not only for their anti-plaque effects, as is the case with previous articles, but for their effects on cavities, gingival condition, oral pathologies as well as bad odors.

4.3.4. Zinc and Periodontitis

Zinc deficiency has been suggested to be a potential risk factor for oral and periodontal diseases.

In vitro experimental studies on rats on a zinc-deficient diet demonstrated a higher plaque index in this category. These rats also developed parakeratosis in the normally keratinized back of the tongue. Hyperkeratinization was observed in the valleys between the papillae [40].

Regarding gingivitis, the use of toothpastes containing zinc has proven positive effects in reducing plaque and gingival inflammation [32].

4.3.5. Zinc and Oral Lichen Planus (See Figure 4)

Much attention has been paid to metals as allergic causes of this pathology. Additional evidence was needed to prove that zinc may be a causative allergen of oral lichen planus [41].

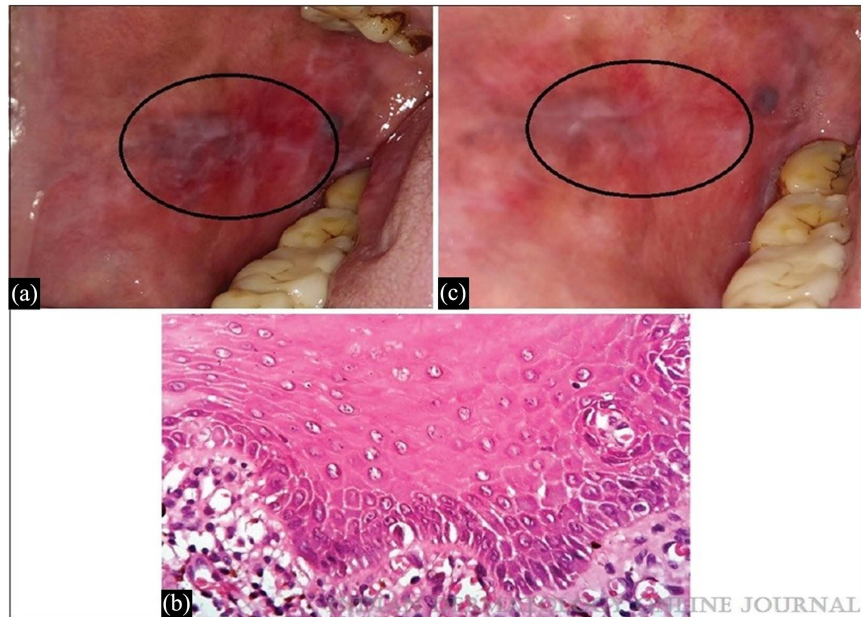


Figure 4. Reduction in the size of oral Lichen planus lesions after zinc treatment [18]. (a). Erosive lesions of lichen planus on the buccal mucosa. (b). Histological section of the jugal mucosa, before treatment of the lesion, stained with haematoxylin and eosin showing hyperkeratotic epithelium and fibrocellular underlying connective tissue stroma with spongiosis and acanthosis in the circled areas (x400). The underlying connective tissue is fibrocellular with dense inflammatory cells (mainly lymphocytes). (c). Reduction in the erosive pattern of lesions after treatment with zinc supplementation on the jugal mucosa.

4.3.6. Zinc and Dysgeusia

The use of polaprezinc improves parakeratosis and reduces the proliferation of taste bud cells caused by zinc deficiency.

These effects could be involved in the underlying mechanisms thus improving taste disorders in animal models [42].

4.3.7. Zinc and Burning Mouth Syndrome

Burning mouth syndrome refers to mouth pain, usually involving the tongue, in people who have no visible lesions or abnormalities in the mouth. Zinc deficiency could be an etiological factor in some patients with this condition. In these patients. Appropriate zinc replacement therapy has been shown to be effective in relieving symptoms [43].

4.4. Use of Zinc in Dentistry

- Studies have demonstrated that immersing gutta percha cones in zinc oxide increases their antibacterial activity and maintains appropriate cytocompati-

bility with human cells [44].

- Studies on composite resins and glass ionomers containing zinc have demonstrated high antibacterial properties. By inhibiting the growth of *Lactobacillus* and *Streptococcus mutans* while respecting mechanical properties such as flexural strength, compressive strength and micro-shear bond strength [45] [46].
- During orthodontic treatment, a frictional force between the bracket (or brackets) and the wire is unstoppable in the sliding procedure. This force creates the risk of root resorption and anchoring difficulties.
- According to an in vitro study evaluating the orthodontic friction force in sliding techniques. It has been noted that a 17% reduction in force occurs when the bracket is coated with zinc [47].
- Zinc-hydroxyapatite solutions significantly reduce the loss of enamel micro hardness caused by cold light bleaching and maintain the enamel surface almost intact [48].
- In a systematic review by Moradpoor et al, it was shown that exposure of bone to zinc nanoparticles has antimicrobial properties, inhibiting bacterial colonisation. This reveals the possibility of applying zinc in nanoparticle formulations for tissue engineering. This can accelerate bone regeneration, inhibit biofilm formation and promote osseointegration of implants [49].
- The addition of zinc in dental adhesive creams ensures the elimination of bacteria linked to bad oral odors. A series of case studies have reported that patients developed progressive myelopolyneuropathy after prolonged and excessive use of zinc-containing adhesives. Although the evidence remains at the case report level and without being able to determine exactly the amount of denture adhesive ingested/zinc absorbed, the relationship between copper deficient myelopathy and denture adhesive containing zinc remains an assumption [50] [51].

4.5. Different Zinc-Containing Dental Materials

4.5.1. Dental Sealants

1) Definitive cementation materials

The main materials used for permanent dental sealants are zinc phosphate and zinc polycarboxylate cement.

Zinc phosphate has a non-adhesive bond, reaching maximum physical properties after 24 hours. Its compressive strength is very high, while its tension strength remains low compared to other sealing cements. It has a high modulus of elasticity and a fairly high early solubility, which decreases as the material ages [52].

Two desirable properties of this sealing agent are a degree of adhesion to the preparation and favourable biocompatibility.

2) Root canal sealants

- Zinc oxide-eugenol or ZOE sealants contain zinc oxide powder, liquid euge-

nol and an essential oil derived from cloves.

- Zinc oxide-eugenol cements have better antimicrobial effects in a zone of inhibition test for *Streptococcus mutans*, *Staphylococcus aureus* and *Enterococcus faecalis* than many epoxy resin sealants. This property is mediated by zinc oxide, which is a well-documented antimicrobial material that interferes with bacterial membrane proteins [53].
- Like zinc oxide-eugenol cement, zinc oxide-propolis cement propolis cement contains zinc oxide combined with propolis. Propolis is a resinous compound with antimicrobial, anti-inflammatory, anticancer, antifungal and antiviral properties.
- Comparing all the parameters, zinc oxide-propolis appears to be the best root canal filling material. It has demonstrated very low rates of pain, swelling, draining fistula and mobility compared to other root canal sealants [54].

4.5.2. Materials for Definitive Dental Restorations

1) Amalgam

The zinc-containing amalgams have demonstrated superior resistance to fatigue and creep. They resist marginal fracture and fatigue crack propagation during traction. However, studies have noted that amalgam presents a toxicity linked to the release of zinc, when placed in contact with neural cells it causes toxic effects, but a clear dose-dependent toxicity has not been established [55] [56].

2) Composite resins containing zinc oxide

Inorganically filled dental composite resins are widely used in dentistry because of their high aesthetic properties as fillings, their mechanical strengthening in restorative procedures and their ability to bind in a single layer.

Zinc oxide has been introduced into the composition of certain dental composites due to its antibacterial potential, which occurs via the release of zinc ions into the growth media [45] [49].

4.6. Clinical Implications and Prospects

In the light of current discoveries, it would seem possible to explore and optimise the therapeutic potential of zinc, not only as an antibacterial agent, but also as a possible preventive treatment for caries. Zinc and phosphate appear to be important for the homeostasis of hydroxyapatite and it could help achieve a balance between the demineralisation and remineralisation processes in dental tissue [3].

It has been noted that the inclusion of zinc-dentin adhesive systems should be further investigated as a safe mechanism to increase the longevity of resin-dentin bonding interfaces. zinc has the potential to usher in a new era of interest in the development of cost-effective and valuable oral health products, including various toothpaste and mouthwash formulations [4] [5].

Zinc deficiency is associated with the pathogenesis of common diseases of the oral mucosa as well as other diseases. A healthy diet rich in zinc and other mi-

cronutrients is therefore essential to optimise oral and dental health. However, further research studies and the conduct of well-designed randomised clinical trials that focus on supplementation with the intention of using the zinc as an adjunctive treatment for oral disease are still needed [16] [18].

5. Conclusions

Zinc is a trace element of great importance in the oral cavity. It is naturally present in various places such as dental plaque, dental hard tissue and saliva and it is highly effective against hard tissue demineralisation and plays an important role in dentine remineralisation. In terms of dental plaque, zinc controls plaque formation and inhibits tartar formation.

Zinc salts are used in various products for oral use, such as mouthwashes and toothpastes, for their anti-bacterial effectiveness, their ability to cleanse the gums and periodontium, and their reduction in the volatile sulphur compounds that cause halitosis. As for oral pathologies, zinc therapy has proved effective in the treatment of oral lichen planus, recurrent aphthous stomatitis and pathologies linked to chemotherapy or radiotherapy. It is also effective in treating dysgeusia. A number of articles have demonstrated the antioxidant and, above all, antibacterial effects of zinc, which is why it is used in dental sealants and root canal fillings, as well as in orthodontic materials and equipment. However, further research studies are still needed to determine the effect of zinc supplementation in the treatment of oral diseases. In addition, in vitro experiments are essential to find a balance between antibacterial and mechanical efficacy in the new zinc-based nanotechnology.

Conflicts of Interest

The authors declare no conflicts of interest.

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