KOWALSKA, Klaudia, WERONIKA KIEŁT, JULIA KOZŁOWSKA, GABRIELA BRONIEC, BARBARA WAJDOWICZ, ALEKSANDRA KUDŁA, ROZALIA CZAPIEWSKA, ALEKSANDRA DZIEWULSKA, ALEKSANDRA WRÓBEL and LAURA PACEK. Is fluoride the best we've got? The most common toothpaste active ingredients and their influence on caries and oral health: A brief review of the literature. Journal of Education, Health and Sport. 2024;64:55477. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2024.64.55477
https://apcz.umk.pl/JEHS/article/view/55477

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).© The Authors 2024;
This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.09.2024. Revised: 10.09.2024. Accepted: 06.10.2024. Published: 07.10.2024.

Is fluoride the best we've got? The most common toothpaste active ingredients and their influence on caries and oral health: A brief review of the literature

Klaudia Kowalska

Łukasz Bańczyk Specialist Dental Practice, 166 Jana Kilińskiego St., 42-218 Częstochowa, Poland

ORCID 0009-0001-5240-7983

https://orcid.org/0009-0001-5240-7983

E-mail: kowalska.dent@gmail.com

Weronika Kiełt

Medical University of Lublin, located at Aleje Racławickie 1, 20-059 Lublin, Poland

ORCID 0000-0002-1933-6271

https://orcid.org/0000-0002-1933-6271

E-mail: weronika.kielt@gmail.com

Julia Kozłowska
Medical University of Lublin, located at Aleje Racławickie 1, 20-059 Lublin, Poland
ORCID 0000-0002-6161-970X
https://orcid.org/0000-0002-6161-970X
E-mail: kozlowskajulia14@gmail.com

Gabriela Broniec
Non-public Healthcare Facility, Neodent Dental Clinic, located at 15 Wallenroda St., 20-607 Lublin, Poland
ORCID 0009-0006-6615-3677
https://orcid.org/0009-0006-6615-3677
E-mail: gaba9809@o2.pl

Barbara Wajdowicz
Non-public Healthcare Facility, Em-Dent Dental Clinic, located at 11 Weteranów St., 20-038 Lublin, Poland
ORCID 0009-0006-1754-6124
https://orcid.org/0009-0006-1754-6124
E-mail: baswaj2@gmail.com

Aleksandra Kudła
Medical University of Gdansk, located at 3a Marii Skłodowskiej-Curie St., 80-210 Gdańsk, Poland
ORCID 0009-0005-8734-8310
https://orcid.org/0009-0005-8734-8310
E-mail: k.aleksandra.xoxo@gmail.com

Rozalia Czapiewska
Medical University of Gdansk, located at 3a Marii Skłodowskiej-Curie St., 80-210 Gdańsk, Poland
ORCID 0009-0002-8198-471X
https://orcid.org/0009-0002-8198-471X
E-mail: rozalia.czapiewska@tlen.pl

Aleksandra Dziewulska
Non-public Healthcare Facility, Lekarze Specjalisci LLC, 7 Topolowa St., 20-352 Lublin, Poland
ORCID 0000-0001-6405-409X0000-0001-6405-4090000-0001-6405-409
https://orcid.org/0000-0001-6405-409X
E-mail: aleksandradziewulska01@wp.pl

Aleksandra Wróbel
Chair and Department of Public Health, Medical University of Lublin, 1 Chodźki St., 20-093 Lublin, Poland
ORCID 0009-0007-6104-3804
https://orcid.org/0009-0007-6104-3804
E-mail: aawrobel.98@gmail.com

Laura Pacek
Non-public Healthcare Facility, Lekarze Specjalisci LLC, 7 Topolowa St., 20-352 Lublin, Poland
ORCiD 0000-0001-6069-7653
https://orcid.org/0000-0001-6069-7653
E-mail: paceklaura@gmail.com

ABSTRACT:

Aim of the study

Toothpaste is a paste or gel to be used with a toothbrush to maintain and improve oral health and aesthetics. Nowadays there is a great variety of ingredients that might have different effects on caries development or oral health in general. Society continues to seek ways to replace fluoride or include more natural ingredients in everyday hygiene products. The aim of our study is to present current knowledge of various ingredients in toothpastes regarding their influence on teeth and intraoral soft tissues and the possibility of replacing fluoride with other substances.

Material and methods

Our review is based on the analysis of materials collected in„Pubmed", „Google Scholar" and other scientific articles using keywords: „toothpaste", „fluoride", „ingredients",

“hydroxyapatite”, „chlorhexidine”, “triclosan”, “propolis”, “aloe vera”, “charcoal”, “oleanolic acid”, “SLS”, “xylitol”

Conclusions

Despite numerous studies, there is space for further research in finding substances that might improve toothpastes with or without extracting fluoride from them. Fluoride has the most proven effectiveness in caries prevention, with fluorosis as its most damaging side effect, while hydroxyapatite shows promising results. Although, there are many substances that might be useful in oral health care products.

Key words: “toothpaste”; “oral health products”; “toothpaste ingredients”; “fluoride”

Introduction

The 2015 Global Burden of Disease (GBD) Study took under consideration 313 diseases and found untreated dental caries in permanent teeth to be the most prevalent condition, with 2.3 billion people affected, while in comparison 7.8% children has been experiencing the disease in deciduous teeth.[1] The process of dental caries development starts with colonisation of susceptible tooth surface with cariogenic bacteria, mostly mutans streptococci, lactobacilli or Veillonella, and concurrent presence of dietary sucrose or refined sugar. Bacterial pathogens metabolize carbohydrates, producing lactic acid which dissolves the hydroxyapatite crystal structure of the tooth. [2], [3] The formation of a cavity occurs when the diffusion of calcium, phosphate and carbonate out of the tooth is permitted to continue.[4]

- **Fluoride**

With no doubt fluorides play a pivotal role in both prevention and control of dental caries and the discovery of its anti-cariogenic properties represents one of the most significant landmarks in the history of dentistry. Although, both earlier theories with the evolution of scientific knowledge explaining the possible causal effects of fluoride on teeth (and bone) provides an excellent example of the necessity for changing concepts in medicine in order to improve health. [5]

Various forms of fluorides are available for topical application, including toothpastes, gels, foams, varnishes, and mouth rinses. Over the years, different fluoride compounds have been used, such as stannous fluoride (SnF_2), sodium fluoride (NaF), sodium monofluorophosphate (SMFP), acidulated phosphate fluoride (APF), and amine fluoride (AmF).The first clinically proven anti-caries toothpaste, introduced in 1950, contained stannous fluoride (SnF_2). SnF_2

remains superior to other fluoride compounds due to its broad-spectrum antimicrobial properties, particularly against dental plaque and gingivitis. The stannous ion (Sn^{2+}), the active form in SnF_2, demonstrates significant antiplaque effects by inhibiting bacterial metabolism and reducing bacterial virulence and biomass. Sn^{2+} ions have shown a more effective plaque-inhibiting effect than stannic ions (Sn^{4+}), underscoring the importance of maintaining the Sn^{2+} state in toothpaste and mouth rinse formulations for maximum efficacy.

Sodium fluoride (NaF), the simplest fluoride compound, is prevalent in most toothpastes. NaF exerts a bacteriostatic effect, where free fluoride ions (F^-) from dissociated NaF penetrate bacterial cell membranes, disrupting bacterial metabolism. This mechanism contributes to its widespread use in caries prevention.

Fluorides are considered the most critical active ingredient in toothpaste, with fluoride toothpastes being the most widely used method for maintaining a consistently low level of fluorides in the oral cavity. While fluorides are essential for caries prevention, chronic daily ingestion of fluoride levels exceeding 1 mg/L or 0.1 mg/kg during tooth development can lead to dental fluorosis. Dental fluorosis is characterized by the formation of hypomineralized enamel. Clinically, dental/enamel fluorosis manifests as mild opaque white or brown mottling of the enamel, often accompanied by pits and enamel fractures in both deciduous and permanent teeth.

The generally accepted fluoride concentration in toothpastes ranges from 1000 to 1500 ppm. [19]

To understand fluoride importance in caries control it’s important to understand its mechanism.

It is recommended that oral hygiene instructions focus on regular, gentle biofilm destruction rather than meticulous removal. Fluoride plays a key role in biofilm control, as it is present in the biofilm around the clock. Fluoride can reduce the sugar stress of the biofilm by lowering the critical pH required to dissolve enamel, thereby reducing demineralisation. Furthermore, fluoride can inhibit numerous features associated with dental caries, including enzymes involved in biofilm matrix production and enolase. This directly slows glycolysis and indirectly reduces bacterial sugar transport systems. A recent study demonstrated that fluoride exposure resulted in a significant inhibition of sugar metabolism in oral biofilms, followed by a reduction in saccharolytic organisms. This confirms the beneficial effects of fluoride-containing oral hygiene products.[6]

The differing anatomy, histology, and chemical composition of dental tissues may result in a heightened risk of caries development on root surfaces relative to coronal surfaces.[7] On the

subject of root decay, fluoride interventions are consistently recognized as highly beneficial for controlling caries, supported by robust evidence. However, there remains a scarcity of data concerning the relative preventive and therapeutic effects of fluoride on dentin. Research suggests that tooth brushing with high-fluoride dentifrice (5000 ppm F) may offer superior efficacy in controlling root caries. Nevertheless, toothpastes with such high fluoride concentrations are restricted to prescription-only access from dentists. An alternative strategy involves combining a standard fluoride dentifrice (1100 ppm F) with professional fluoride applications, such as fluoride varnish, fluoride gel, or 38% silver diamine fluoride. Consequently, the current recommendation for root caries prevention emphasizes the importance of access to dental care. Moreover, the efficacy of fluorides in preventing and remineralizing tooth surfaces relies on the presence of calcium and phosphate ions. Therefore, it is envisaged that caries preventive formulations supplemented with additional calcium and phosphate ions to enhance saliva's preventive potential may prove more effective in preventing root caries.[8]

- **Hydroxyapatite**

Scientists have been engaged in an ongoing endeavour to identify a substitute to fluoride, given the potential drawbacks associated with its use. There are a number of reasons why hydroxyapatite toothpastes could be a suitable alternative to fluoride toothpastes. Hydroxyapatite is considered to be a safe active ingredient. Fluoride, however, can cause dental fluorosis, which has been documented even in areas of low fluoride content in the drinking water.[9]

When comparing the two, fluoride remineralization is limited to the surface layer of the lesion, while HAP remineralization seems to be deeper and homogenous throughout the subsurface layer of the lesion.[15]

A recent in situ study proves that the application of 5% nanoHAP-containing dental lotion immediately following toothbrushing with 5% nanoHAP toothpaste enhances the efficacy of the nanoHAP toothpaste in remineralizing initial caries lesions.[10]

The hope for a new golden agent is raised by another study in which 10% hydroxyapatite achieved comparable efficacy to 500 ppm F - in remineralising initial caries and preventing demineralisation. Thus, this study confirms that HAP toothpaste is equal to fluoride toothpaste.[11] Hydroxyapatite may be a particularly suitable active ingredient for individuals where high fluoride exposure is contraindicated, including children who are at risk of swallowing it, pregnant women, and individuals affected with hyposalivation, which results in

lack of calcium and phosphate ions for remineralisation.[12]

Another property of hydroxyapatite supports its predominance as an ingredient in toothpastes. The nanostructured hydroxyapatite micro-particles exert a coating effect, reintegrating the enamel with a biomimetic film that reproduces the structure and morphology of the biological hydroxyapatite of the enamel.[13] Deposition of HAP particles in micro- or nanocrystalline form that Hydroxyapatite toothpastes contain hydroxyapatite particles in micro- or nanocrystalline form, which have been shown to bind to enamel surfaces to deposit and restore demineralised surface defects and micropores. Naturally occurring enamel consists of 20-40 nm diameter HAP nanoparticles and it is suggested that the use of 20 nm diameter HAP nanoparticles effectively regenerates damaged enamel.[14]

Continuous influx of hydroxyapatite particles from oral care products results in the densification and renewal of the adhering layer, thereby argumenting its protective characteristics. Nevertheless, HAP is not solely responsible for the formation of a protective layer at the exposed surfaces of teeth; it can also be built into dental biofilm. The benefit of this occurrence begins with dissolution of particulate HAP by acids derived from either food or bacteria, which results in the release of calcium ions and an increase in plaque pH.

Consequently, there are a number of advantages to be gained. Aforementioned acids don't attack the tooth surface because of the protective HAP layer it attacks first having enamel protected. Calcium released from dissolved hydroxyapatite remineralizes demineralized parts of enamel also in its deeper layers, not only on the surface.

Continuously, calcium concentration increase brings HAP back from dissolution to it's more solid state and increases pH making it more difficult for demineralisation to happen as the critical pH of enamel is 5.5. [15] HAP additionally improves tooth colour.[16]

To acknowledge HAP benefits in toothpastes, it's important to examine its beneficial properties in other formulas- such as mouthwashes. The number of bacteria reduced on tooth surfaces after the use of HAP mouthwashes is comparable to that observed with 0,2% chlorhexidine, so it's safe to say hydroxyapatite causes inhibition of bacterial plaque adhesion. From a clinical point of view the mouthrinse based solely on hydroxyapatite particles appears to be a promising chlorhexidine substituting option to effectively control bacterial biofilm formation as everyday use products. A study in situ showed that hydroxyapatite aggregates accumulate at the tooth surface as well as to salivary bacteria. The adherence of HAP particles by bacteria facilitates the formation of aggregates that are readily cleared from the oral cavity through the action of saliva and oral rinsing, in conjunction with the removal of loose particles. This study raises hopes for further exploration of applications for hydroxyapatite

particles and its use as the gold standard in daily oral hygiene.[17]

- **Chlorhexidine**

Chlorhexidine (CHX) is a bisbiguanide that prevents the growth of bacteria and has bactericidal effects.[18,19] It is the most studied and most effective anti-plaque and anti-gingivitis agent and is considered the "gold standard" anti-plaque product, a broad-spectrum antiseptic effective against gram-positive and gram-negative bacteria, yeasts, and viruses. Chlorhexidine's mechanism of action depends directly on its dose- it is bacteriostatic at very low concentrations (0.02–0.06%) and bactericidal at higher concentrations (0.12–0.20%). Except its immediate bactericidal effect, CHX also exhibits prolonged, slow anti pathogenic effect by aggregating to the oral mucosa.[19] Plaque, gingival and bleeding scores improve with use of a toothpaste containing 1% CHX.[20] Toothpastes containing CHX must be sodium lauryl sulfate (the foaming agent)-free because interaction between the two reduces the beneficial effects of fluoride on the remineralization of enamel lesions.[21] Nevertheless, chlorhexidine is not a perfect antiseptic as it brings many side effects, the most common are parotid gland swelling, pigmentation of the oral soft tissues and teeth. It also causes increased calculus formation and change of taste sensation. Other less frequent effects are a burning sensation, mucosal lesions and anaesthetized sensation.[22,23] A study presented a 58-year-old man with a well-demarcated erythematous area on the right upper anterior gingiva, which appeared immediately after the first application chlorhexidine digluconate gel with intense burning sensation and proved to be a hypersensitivity reaction on CHX.[23]

- **Triclosan**

A much valued antimicrobial is triclosan (TCS). It was first used at hospitals in 1972 and since then it became a part of many everyday use hygiene products, such as soaps, hand sanitizers, toothpaste or mouthwash.[26]

TCS creates many benefits as a toothpaste ingredient. Its 0.3% addition to toothpastes with polyvinyl methyl ether and maleic acid copolymer twice a day creates a more effective plaque control and gingival health in comparison to a conventional toothpaste with fluoride, while not providing greater dentin sensitivity. Furthermore, when triclosan is used along with fluoride, it does not only lower plaque accumulation, gingival inflammation, but also reduce gingival bleeding in comparison to ordinary fluoride toothpaste.[24] A 5-year-long study on patients with established cardiovascular disease suggests that using a toothpaste with triclosan significantly slowed progression of periodontitis, yet it did not have great influence on key

subgingival periodontopathic bacteria.[25] With time more and more studies on triclosan appeared. Some of them reported triclosan to be a chemical substance disrupting functioning of the endocrine system in many species, including humans. Moreover, TCS is associated with cancer development, which was proved in mouse liver, where it caused proliferation of hepatocytes and reactive oxygen species production, so in conclusion it acts as a liver tumor promoter. Moreover, in mice it had impairing influence on cardiovascular system by decreasing its functions. Same impact was observed in both mice and fathead minnows with muscle function. TCS reduced grip strength and swimming abilities in either species, respectively. Naturally, the most disturbing studies were presented on humans. This antibacterial is shown to be correlated with spontaneous abortion rates, when high TCS urine concentration is presented. Also patients exposed on TCS may demonstrate allergies and asthma symptoms. All these deeply concerning adverse effects resulted in banning this product recently by the Food and Drug Administration (FDA), but only from certain soap products. Despite its various downsides, Triclosan remains a part of many commonly available and widely used products, including a well-known toothpaste.[26]

- **Calcium phosphate**

Calcium phosphate is a name for many different chemical compounds. Chemically, they are salts of orthophosphoric acid, H3PO4. The most important calcium phosphates in biology and food technology are monocalcium phosphate Ca(H2PO4)2 (MCP), dicalcium phosphate CaHPO4 (DCP), tricalcium phosphate Ca3(PO4)2 (TCP), and pentacalcium phosphate (better known as hydroxyapatite; HAP, mentioned earlier), Ca5(PO4)3OH. Some of these forms are often mistaken for one another in statements presented to others by putting them in the same category.[27]

Therefore, some forms of calcium phosphate are highlighted for the need of this review.

Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP) is used often in dentin hypersensitivity reduction, in the bleaching process. When used in toothpaste it also has the same effect and to add on it reverses white spot lesions, protects against dental erosion and does not interfere with bleaching in the meantime.[16]

Calcium Sodium Phosphosilicate (CSPS, Novamin, Biomin, Bioglass) alone is proved to remineralize the softened enamel, but along with fluoride added to the toothpaste, it shows better results. [28] CSPS also reduces dentin hypersensitivity and can control gingival health.[16]

Studies on Beta-Tricalcium Phosphate (β-TCP) are still needed, but those conducted are quite promising. They present that TCP toothpastes can reduce caries as well as fluoride ones and

also helps with dentin hypersensitivity.[16]

- **Propolis**

Propolis is 50% to 60% resin, 30% to 40% wax, 5% to 10% essential oils, 5% pollen, along with some microelements. Its antimicrobial effect works against Streptococcus mutans , facultative anaerobes, and Gram-positive cocci within the oral cavity. In addition, it's proven to kill periodontal pathogens. Propolis has significant positive effects on gingival health, oral hygiene, and the reduction of pathogenic bacteria. It's not quite resolved which chemical compounds of propolis are responsible for it's good properties.[29] One study presented that certain compounds derived from propolis have bacteriostatic activities while other compounds have bacteriocidal properties against various oral species including Porphyromonas gingivalis.[30] To sum up, it has antibacterial, anti-inflammatory, antifungal, antiviral, anticancer, and immunomodulation abilities, so it's very promising as a part of oral care products.[29]

- **Aloe vera**

Toothpastes with fluoride have one of the highest remineralization effect among others, however, an in vitro study presented that aloe vera increases remineralization effect when used with high-concentration fluoride toothpastes. It can be an outcome of the synergic reaction between aloe vera and sodium monofluorophosphate promoting remineralization.[31]
Toothpastes with natural ingridients were compared. Products with aloe vera, same as propolis, showed to provide antibacterial effect only on Streptococcus mutans.[32] Studies on aloe vera reducing dental plaque and gingivitis are inconclusive. Some present antiplaque and antigingivitis effect, while the others do not show any improvement in GI and PI scores. There are voices, however, as it may be used as an alternative to chemical toothpaste.[33]

- **Charcoal**

Charcoal-based toothpastes have been shown to increase surface roughness in enamel.[34] A study in vitro on human permanent incisors was performed. Teeth were first stained and then tested with 4 different charcoal-based toothpastes. The study proved that the colour, after 12 weeks of brushing the teeth twice a day, didn't improve. One of the four increased teeth's microhardness, while three out of four led to an increase in surface roughness. They didn't cause more than a few scratches, however.[34] Charcoal not only is unhelpful in whitening teeth, but can also contribute to worsening of patients' smiles. In people with periodontal disease,

with deep pockets, charcoal can accumulate in them and effect in grey or even black spots in gums. Some people were led to believe absorption capabilities of activated charcoal might help with the halitosis problem. Charcoal does not address the underlying causes of halitosis. Moreover, it's absorbative properties might cause lower effect of flavourings, essential oils or other toothpaste ingredients, which help cover the smell coming from oral cavity.[35]

- **Oleanolic acid**

Oleanolic acid is of natural origin, it is found in many fruits, vegetables and commonly used herbs. OA improves lipid metabolism, glycemic control and exhibits much potential in prevention of chronic cardiovascular diseases, cancer or diabetes. [36] When presented with many positive properties, OA had to be tested in dentistry. Toothpaste containing 0,1% oleanolic acid has the same reduction in gingival index score as 0,12% chlorhexidine mouthwash. However, it's antiplaque and antigingivitis effect isn't better than toothpaste's with fluoride.[37] OA presents anti-bacterial activity against oral pathogens- Streptococcus mutans, Actinomyces viscosus, P. gingivalis, and P. intermedia.[38]

- **SLS (Sodium Laureth Sulfate)**

Sodium Laureth Sulfate has already been mentioned earlier in this review, as a widely used addition to many detergents.

There should be no issue with the use of CHX mouthwash in combination with an SLS dentifrice, irrespective of the order of use. It would seem that the use of CHX mouthwash does not appear to interfere with the efficacy of the SLS dentifrice in inhibiting dental plaque.[39]

A study examining the efficacy and impact on oral health of a dentifrice containing SLS compared to one without it showed that the first one causes fewer soft tissue problems, at the same time being just as effective at stopping the production of acids by cariogenic bacteria, thereby reducing the formation of caries as well as a toothpaste with fluoride that's SLS free.[40]

- **Xylitol**

Xylitol has been widely recognized and scientifically demonstrated as a safe and effective agent for the prevention of tooth decay when it is used consistently as part of a regular oral care routine. However, despite its proven efficacy, the widespread application of xylitol has been somewhat restricted due to the lack of available formulations that require minimal

patient adherence while remaining both acceptable and safe, particularly in environments where the use of chewing gum might be prohibited or impractical. The existing body of substantial literature suggests that, in order to achieve a clinically significant effect, it is generally necessary to consume a minimum of five to six grams of xylitol, with at least three exposures per day, typically obtained through products like chewing gum or candies. At the same time, there is conflicting evidence in the scientific literature from studies involving toothpaste, which suggests that lower doses of xylitol, combined with less frequent exposures, might still be effective in preventing tooth decay. Additionally, the increasing trend of using xylitol as a sweetener in small quantities within various foods and other consumables is concurrently raising the overall exposure of the general public to xylitol, potentially leading to additive oral health benefits over time.[41]

A study conducted utilizing the Quantitative Light-induced Fluorescence (QLF) method yielded significant findings that demonstrated a notable enhancement in the remineralization of enamel when using a toothpaste slurry containing 500 ppm fluoride (F-) combined with 5% xylitol, compared to a similar formulation without the addition of xylitol. These results suggest that the inclusion of xylitol in toothpaste formulations can lead to improved remineralization of enamel. While it is important to acknowledge that these findings cannot be directly and unequivocally extrapolated to in vivo situations due to the inherent limitations of in vitro studies, the data suggests that toothpaste containing 500 ppm fluoride (NaF) along with 5% xylitol may offer potential benefits. Specifically, this combination might be advantageous in terms of its caries-inhibiting effects, while simultaneously reducing the risk of dental fluorosis, particularly in young individuals who are in the process of undergoing enamel remineralization.[42]

The literature review also concluded that the most effective xylitol product for caries prevention was pure (100%) xylitol, which was most beneficial when chewed or consumed three to five times daily, particularly after meals, with a total daily intake ranging from 5 to 10 grams of xylitol. The products evaluated in the review included xylitol-containing lozenges, candies, and chewing gum, as well as foods made with xylitol, and oral care products such as xylitol-containing toothpaste and mouth rinse. The results consistently demonstrated that products containing xylitol significantly outperformed other non-xylitol control products in preventing dental caries.[43]

Summary

This paper briefly reviews various active ingredients commonly found in toothpaste and their

effects on dental caries and overall oral health. The study emphasises fluoride's established efficacy in preventing caries but also explores potential alternatives like hydroxyapatite, which may offer similar benefits without the risk of dental fluorosis. The review highlights the role of xylitol and hydroxyapatite in caries prevention and examines other ingredients such as chlorhexidine, triclosan, and natural substances like aloe vera and propolis. The article suggests that while fluoride remains the most proven agent, there is potential for other ingredients to play a significant role in oral health care products.

Author's contribution

Conceptualization, KK, and BW; methodology, KK, BW, and WK; software, LP, AW, AD, BW, RC and AK; check, KK, GB and JK; formal analysis, KK, BW, RC, JK, LP, AW; investigation, LP, AD, and BW; resources, KK, and BW; data curation, KK, AD; writing-rough preparation, KK, JK, BW, WK, AK, RC; writing - review and editing, KK, BW, AK, WK, LP, GB, AD, AW; visualisation, GB, AW; supervision, KK and AW; project administration, KK, BW; All authors have read and agreed with the published version of the manuscript.

Funding Statement

The article did not receive any funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Acknowledgements

Not applicable.

Conflict of Interest Statement

Authors declare no conflicts of interest.

References

1. Kassebaum NJ, Smith AGC, Bernabé E, et al. Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990–2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. *J Dent Res*. 2017;96(4):380-387. doi:10.1177/0022034517693566

2. Caufield PW, Griffen AL. DENTAL CARIES: An Infectious and Transmissible Disease. *Pediatr Clin North Am*. 2000;47(5):1001-1019. doi:10.1016/S0031-3955(05)70255-8

3. Valm AM. The structure of dental plaque microbial communities in the transition from health to dental caries and periodontal disease. *J Mol Biol*. 2019;431(16):2957-2969. doi:10.1016/j.jmb.2019.05.016

4. Selwitz RH, Ismail AI, Pitts NB. Dental caries. *The Lancet*. 2007;369(9555):51-59. doi:10.1016/S0140-6736(07)60031-2

5. Fejerskov O. Changing Paradigms in Concepts on Dental Caries: Consequences for Oral Health Care. *Caries Res*. 2004;38(3):182-191. doi:10.1159/000077753

6. Pitts NB, Twetman S, Fisher J, Marsh PD. Understanding dental caries as a non-communicable disease. *Br Dent J*. 2021;231(12):749-753. doi:10.1038/s41415-021-3775-4

7. Ravald N. Root surface caries. *Curr Opin Periodontol*. Published online 1994:78-86.

8. Amaechi BT, Phillips TS, Evans V, et al. The Potential of Hydroxyapatite Toothpaste to Prevent Root Caries: A pH-Cycling Study. *Clin Cosmet Investig Dent*. 2021;13:315-324. doi:10.2147/CCIDE.S319631

9. Paszynska E, Pawinska M, Enax J, et al. Caries-preventing effect of a hydroxyapatite-toothpaste in adults: a 18-month double-blinded randomized clinical trial. *Front Public Health*. 2023;11:1199728. doi:10.3389/fpubh.2023.1199728

10. Amaechi BT, Alshareif DO, Azees PAA, et al. Anti-caries evaluation of a nano-hydroxyapatite dental lotion for use after toothbrushing: An *in situ* study. *J Dent*. 2021;115:103863. doi:10.1016/j.jdent.2021.103863

11. Amaechi BT, AbdulAzees PA, Alshareif DO, et al. Comparative efficacy of a hydroxyapatite and a fluoride toothpaste for prevention and remineralization of dental caries in children. *BDJ Open*. 2019;5:18. doi:10.1038/s41405-019-0026-8

12. Enax J, Fabritius HO, Fabritius-Vilpoux K, Amaechi BT, Meyer F. Modes of Action and Clinical Efficacy of Particulate Hydroxyapatite in Preventive Oral Health Care − State of the Art. *Open Dent J*. 2019;13(1):274-287. doi:10.2174/1874210601913010274

13. Bossù M, Saccucci M, Salucci A, et al. Enamel remineralization and repair results of Biomimetic Hydroxyapatite toothpaste on deciduous teeth: an effective option to fluoride toothpaste. *J Nanobiotechnology*. 2019;17:17. doi:10.1186/s12951-019-0454-6

14. O'Hagan-Wong K, Enax J, Meyer F, Ganss B. The use of hydroxyapatite toothpaste to prevent dental caries. *Odontology*. 2022;110(2):223-230. doi:10.1007/s10266-021-00675-4

15. Meyer F, Enax J, Amaechi BT, et al. Hydroxyapatite as Remineralization Agent for Children's Dental Care. *Front Dent Med*. 2022;3. doi:10.3389/fdmed.2022.859560

16. Limeback H, Enax J, Meyer F. Improving Oral Health with Fluoride-Free Calcium-Phosphate-Based Biomimetic Toothpastes: An Update of the Clinical Evidence. *Biomimetics*. 2023;8(4):331. doi:10.3390/biomimetics8040331

17. Kensche A, Holder C, Basche S, Tahan N, Hannig C, Hannig M. Efficacy of a mouthrinse based on hydroxyapatite to reduce initial bacterial colonisation *in situ*. *Arch Oral Biol*. 2017;80:18-26. doi:10.1016/j.archoralbio.2017.03.013

18. Pankey GA, Sabath LD. Clinical Relevance of Bacteriostatic versus Bactericidal Mechanisms of Action in the Treatment of Gram-Positive Bacterial Infections. *Clin Infect Dis*. 2004;38(6):864-870. doi:10.1086/381972

19. Rajendiran M, Trivedi HM, Chen D, Gajendrareddy P, Chen L. Recent Development of Active Ingredients in Mouthwashes and Toothpastes for Periodontal Diseases. *Molecules*. 2021;26(7):2001. doi:10.3390/molecules26072001

20. Yates R, Jenkins S, Newcombe R, Wade W, Moran J, Addy M. A 6-month home usage trial of a 1% chlorhexidine toothpaste. *J Clin Periodontol*. 1993;20(2):130-138. doi:10.1111/j.1600-051X.1993.tb00327.x

21. Brookes ZLS, Bescos R, Belfield LA, Ali K, Roberts A. Current uses of chlorhexidine for management of oral disease: a narrative review. *J Dent*. 2020;103:103497. doi:10.1016/j.jdent.2020.103497

22. Van Strydonck DAC, Slot DE, Van der Velden U, Van der Weijden F. Effect of a chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review. *J Clin Periodontol*. 2012;39(11):1042-1055. doi:10.1111/j.1600-051X.2012.01883.x

23. Kotsailidi EA, Kalogirou EM, Michelogiannakis D, Vlachodimitropoulos D, Tosios KI. Hypersensitivity reaction of the gingiva to chlorhexidine: case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2020;130(2):156-160.e1. doi:10.1016/j.oooo.2020.04.814

24. The effect of a triclosan/copolymer/fluoride toothpaste on plaque formation, gingivitis, and dentin hypersensitivity: A single-blinded randomized clinical study. Quintessenz Verlags-GmbH. Accessed May 27, 2024. https://www.quintessence-publishing.com/deu/en/article/841002/quintessence-international/2017/02/the-effect-of-a-triclosancopolymerfluoride-toothpaste-on-plaque-formation-gingivitis-and-dentin-hypersensitivity-a-single-blinded-randomized-clinical-study

25. Seymour GJ, Palmer JE, Leishman SJ, et al. Influence of a triclosan toothpaste on periodontopathic bacteria and periodontitis progression in cardiovascular patients: a

randomized controlled trial. *J Periodontal Res*. 2017;52(1):61-73. doi:10.1111/jre.12369

26. Weatherly LM, Gosse JA. Triclosan Exposure, Transformation, and Human Health Effects. *J Toxicol Environ Health B Crit Rev*. 2017;20(8):447-469. doi:10.1080/10937404.2017.1399306

27. Enax J, Meyer F, Schulze zur Wiesche E, Epple M. On the Application of Calcium Phosphate Micro- and Nanoparticles as Food Additive. *Nanomaterials*. 2022;12(22):4075. doi:10.3390/nano12224075

28. Srinivasan N, Kavitha M, Loganathan SC. Comparison of the remineralization potential of CPP–ACP and CPP–ACP with 900 ppm fluoride on eroded human enamel: An in situ study. *Arch Oral Biol*. 2010;55(7):541-544. doi:10.1016/j.archoralbio.2010.05.002

29. Saeed MA, Khabeer A, Faridi MA, Makhdoom G. Effectiveness of propolis in maintaining oral health: a scoping review. *Can J Dent Hyg*. 55(3):167-176.

30. Yoshimasu Y, Ikeda T, Sakai N, et al. Rapid Bactericidal Action of Propolis against Porphyromonas gingivalis. *J Dent Res*. 2018;97(8):928-936. doi:10.1177/0022034518758034

31. Yikici C, Özcan S. Remineralization Activities of Toothpastes with and without Aloe Vera with Different Ratios of Fluoride on Demineralized Enamel: An: In-vitro: Study. *Niger J Clin Pract*. 2022;25(9):1563. doi:10.4103/njcp.njcp_132_22

32. Demir S, Keskin G, Akal N, Zer Y. Antimicrobial effect of natural kinds of toothpaste on oral pathogenic bacteria. *J Infect Dev Ctries*. 2021;15(10):1436-1442. doi:10.3855/jidc.14966

33. Sayar F, Farahmand AH, Rezazadeh M. Clinical Efficacy of Aloe Vera Toothpaste on Periodontal Parameters of Patients with Gingivitis-A Randomized, Controlled, Single-masked Clinical Trial. *J Contemp Dent Pract*. 2021;22(3):242-247.

34. Koc Vural U, Bagdatli Z, Yilmaz AE, Yalçın Çakır F, Altundaşar E, Gurgan S. Effects of charcoal-based whitening toothpastes on human enamel in terms of color, surface roughness, and microhardness: an in vitro study. *Clin Oral Investig*. 2021;25(10):5977-5985. doi:10.1007/s00784-021-03903-x

35. Greenwall LH, Greenwall-Cohen J, Wilson NHF. Charcoal-containing dentifrices. *Br Dent J*. 2019;226(9):697-700. doi:10.1038/s41415-019-0232-8

36. Castellano JM, Ramos-Romero S, Perona JS. Oleanolic Acid: Extraction, Characterization and Biological Activity. *Nutrients*. 2022;14(3):623. doi:10.3390/nu14030623

37. Ramírez GM, Villar CC, Saraiva L, et al. The effect of a toothpaste containing oleanolic acid in reducing plaque and gingivitis: a proof-of-concept randomized trial. *Int J Dent Hyg*. 2021;19(4):450-463. doi:10.1111/idh.12526

38. Olaye T, Tétédé K, Christian K, et al. Natural chemical compounds from plants extract for prevention and treatment of oral infections: a review. *Int J Biosci IJB*. 2022;20:21-38. doi:10.12692/ijb/20.2.21-38

39. Elkerbout TA, Slot DE, Bakker EWP, Van der Weijden GA. Chlorhexidine mouthwash and sodium lauryl sulphate dentifrice: do they mix effectively or interfere? *Int J Dent Hyg*. 2016;14(1):42-52. doi:10.1111/idh.12125

40. Yang M, Zhao HP, Yang J. [Effect of toothpaste containing emulsifier 30 and sodium lauryl sulfate surfactant on the integrity of oral epithelium]. *Shanghai Kou Qiang Yi Xue Shanghai J Stomatol*. 2021;30(3):312-315.

41. Milgrom P, Ly KA, Rothen M. Xylitol and its vehicles for public health needs. *Adv Dent Res*. 2009;21(1):44-47. doi:10.1177/0895937409335623

42. Sano H, Nakashima S, Songpaisan Y, Phantumvanit P. Effect of a xylitol and fluoride containing toothpaste on the remineralization of human enamel in vitro. *J Oral Sci*. 2007;49(1):67-73. doi:10.2334/josnusd.49.67

43. ALHumaid J, Bamashmous M. Meta-analysis on the Effectiveness of Xylitol in Caries Prevention. *J Int Soc Prev Community Dent*. 2022;12(2):133-138. doi:10.4103/jispcd.JISPCD_164_21