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Compositional Analysis and Systemic Considerations of Fluoridated Toothpastes for Children Available in Ankara, Türkiye

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ABSTRACT

Purpose: This study aimed to analyze the composition, fluoride content, and potential health risks of fluoride-containing children's toothpaste available in Turkey. Given the rising concerns over fluoride toxicity and market trends favoring fluoride-free products, the study also evaluated the presence of potentially harmful excipients and assessed their compliance with international pediatric dental guidelines.

Methods: A total of 92 children's toothpaste products were identified through Turkey-based online marketplaces, of which 18 (19.56%) contained fluoride. Fluoride concentrations were classified into 500–990 ppm (9.78%) and 1000 ppm (9.78%), the latter aligning with European Academy of Paediatric Dentistry (EAPD) recommendations. A comprehensive ingredient analysis was performed, categorizing compounds based on their function, prevalence, and toxicity risk. The safety of these ingredients was further assessed using PubMed, ScienceDirect, and Google Scholar databases to determine their documented health effects.

Results: The majority (80.44%) of children's toothpaste products were fluoride-free, raising concerns regarding effective caries prevention. Additionally, fluoridated products contained potentially harmful preservatives (Sodium Benzoate - 44.44%), surfactants (Sodium Lauryl Sulfate - 5.55%), and whitening agents (Titanium Dioxide - 27.77%), all of which have been linked to cytotoxic, irritative, or systemic toxic effects.

Conclusions: These findings highlight a disparity between fluoride availability and professional recommendations, emphasizing the need for improved regulatory oversight, consumer education, and safer pediatric oral care formulations. Given growing concerns about fluoride toxicity, future research should explore fluoride-free remineralization alternatives such as hydroxyapatite and calcium phosphate-based compounds.

Key-words: Children's toothpaste, fluoridated toothpaste, online market, Türkiye

INTRODUCTION

Type Dental caries is the most common oral disease worldwide. The World Health Organization (WHO) estimates that 20% to 90% of 6-year-old children have dental caries.¹ Cavities in children can be a source of

pain and can lead to tooth loss, impaired growth, and developmental failure. Additionally, they can affect speech, appearance, self-esteem, and school performance.² Dental caries are prevalent globally, particularly among adults and children from low

socioeconomic backgrounds. Furthermore, due to disparities in access to dental care, these populations are often overlooked or receive inadequate services in many countries.^{1,2}

The regular use of toothpaste has been associated with a decrease in cavities in many countries. The use of fluoridated toothpaste is found to be beneficial for children and adolescents.³ Since the 1950s, fluoride has been added to toothpaste formulations. It is widely accepted by dentists worldwide that individuals, both children and adults, should be exposed to fluoride through regular use of fluoridated toothpaste.⁴ However, despite the benefits of fluoridated toothpaste, it is considered a risk factor for dental fluorosis. Therefore, the fluoride concentration in toothpaste is extensively debated, especially for children, in order to mitigate the risk of fluorosis.⁵ Some alternatives, such as delaying the use of fluoride-containing toothpaste or using variable fluoride concentrations based on the child's age, have been proposed to reduce the risk of fluorosis.³

There is a lack of consensus among professional organizations regarding recommendations for the use of fluoridated toothpaste.^{5,6} For instance, while Australia is one of the few countries recommending a reduction in fluoride concentration in toothpaste for children under 6 years of age to decrease the incidence of dental fluorosis, many countries advise using fluoridated toothpaste with at least 1000 ppm for children, which is the adult concentration.⁷ This situation is thought to be a result of lower fluoride concentrations in water or higher rates of childhood caries in their respective countries, leading to a prioritization of the caries-preventive effect of higher fluoride doses over the risk of dental fluorosis.^{8,9}

Fluoride is an effective agent in reducing the incidence of dental caries. Therefore, there are no dental organizations advocating for the use of fluoride-free toothpaste nowadays.⁸ In contrast, despite the growing market for herbal and fluoride-free toothpaste, it is expected that the majority of children's toothpaste available in the market will be fluoridated.^{6,10}

Children's specific toothpaste is a relatively new phenomenon, developed both as a way to increase marketability through added flavors, scents, and colorful packaging, and to keep fluoride levels low to reduce the incidence of fluorosis.¹¹ International studies compiling lists of children's toothpaste available in stores have been conducted, revealing the fluoride contents of existing toothpaste.^{3,10, 12, 13} However, there is no similar study available nationwide in Türkiye. This study examines the fluoride levels and contents of toothpaste for children aged 0-6 years available in various markets and platforms across Türkiye.

MATERIAL AND METHODS

This study did not involve the use of human or animal tissues, saliva, organs, or any other materials requiring ethical approval. The research was conducted between September 2024 and December 2024, focusing on the compositional analysis of children's toothpaste products available exclusively in Türkiye-based online marketplaces operating in the Ankara region.

Initially, children's toothpaste products were identified from the oral care sections of major supermarkets in Ankara, Türkiye. The study was later expanded to include only Turkish-based online marketplaces serving the Ankara region. Products were identified using search terms such as "children's toothpaste," "baby toothpaste," and "kids' oral care." To ensure regional specificity, only e-commerce platforms registered in Ankara and shipping within the region were included in the analysis. International e-commerce websites or sellers operating outside Ankara were not considered.

A comprehensive database was created, recording the name, label information, and ingredient list of each toothpaste. A total of 92 different children's toothpaste products were documented and analyzed. Products were categorized into two groups: fluoride-containing and fluoride-free toothpastes. Only fluoride-containing products underwent detailed ingredient analysis.

Following this classification, only the fluoride-containing toothpastes underwent detailed content analysis, focusing on: Fluoride compounds (e.g., sodium fluoride (NaF), amine fluoride (AmF), calcium fluoride (CaF₂)), abrasive agents, preservatives and stabilizers, flavoring and sweetening agents, potential health effects of each ingredient on children.

To assess the safety and effectiveness of fluoride-based formulations, each ingredient was analyzed for its functional role and prevalence across different toothpaste products. Toothpaste ingredient data were recorded in an Excel database. Google Scholar, PubMed, and ScienceDirect databases were utilized to compile scientific data for each component present in the toothpaste formulations.

The quantitative aspect of this study involved calculating the occurrence rate (percentage frequency) of each ingredient across all analyzed fluoride-containing children's toothpaste products. For each ingredient, the presence or absence was recorded. The occurrence rate was calculated by dividing the number of products containing the ingredient by the total number of products analyzed (n = 92). No inferential statistical analyses were conducted; the study employed descriptive statistics only.

The occurrence rate of each ingredient across all toothpaste samples was calculated as a percentage. For

each ingredient, an assessment was conducted to determine:

1. Its role in toothpaste formulation
2. Its potential impact on dental health
3. Any documented health concerns or benefits

All findings were organized into a systematic ingredient-function table, where each component was classified based on its intended function and frequency in the analyzed toothpastes.

Additionally, the fluoride concentrations in these products were compared with the 2019 European Academy of Paediatric Dentistry (EAPD) guidelines to assess compliance with recommended fluoride levels for children.¹⁴

By analyzing the ingredient composition and accessibility of children's toothpaste products, this study aimed to provide a comprehensive quantitative evaluation of fluoride-based toothpaste formulations available in Türkiye, specifically in the Ankara region.

RESULTS

A total of 92 different children's toothpaste products from 42 brands were identified from Türkiye-

based online marketplaces serving the Ankara region. Among these, 18 toothpastes (19.56%) contained fluoride, while 74 toothpastes (80.44%) were fluoride-free (Table 1).

The fluoride-containing toothpaste samples exhibited varying fluoride concentrations: 6 toothpastes (6.52%) contained 500 ppm fluoride, 2 toothpastes (2.17%) contained 990 ppm fluoride, 1 toothpaste (1.09%) contained 700 ppm fluoride, 9 toothpastes (9.78%) contained 1000 ppm fluoride, aligning with the recommended concentration by the EAPD (Table 1).

The predominance of fluoride-free toothpastes raises concerns regarding the accessibility of fluoride-based oral care products and their potential impact on Children's dental health.

The compositional analysis of the fluoridated toothpastes revealed 146 distinct ingredients (Table 1). These ingredients served diverse functions, including cavity protection (fluoride compounds), mechanical cleaning (abrasives), moisture retention (humectants), foaming (surfactants), product stabilization (preservatives), and flavor enhancement (sweeteners).

Table 1. Fluoride Content of Toothpastes

| Fluoride Content | Fluoride Level (ppm) | Toothpaste (n) | Toothpaste (%) |
|------------------|----------------------|----------------|----------------|
| Absent | 0 | 74 | 80,44 |
| Low | 500-990 | 9 | 9,78 |
| Optimal | 1000 | 9 | 9,78 |

Table 2. Ingredients in children's Fluoridated Toothpastes

| Ingredient Type | Occurrence in Flouridated Toothpastes (n) | Function in Toothpaste | Possible Side Effects |
|-------------------------|-------------------------------------------|-----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Amin Flouride | 3 (%16,66) | Cariostatic activity ¹⁵ | Skeletal, dental and some systemic problems ^{15,16} |
| Amyloglucosidase | 1 (%5,55) | Anti-plaque effect, Cariostatic potential ¹⁷ | Mild irritation in sensitive individuals ¹⁷ |
| Anise Alcohol | 1 (%5,55) | Flavoring agent, antimicrobial and anti-fungal activity ¹⁸ | Possible allergic reactions ¹⁸ |
| Aroma | 17 (%94,4) | Sweetener | No specific side effect listed ²² |
| Benzyl Alcohol | 4 (%22,22) | Solvent, antimicrobial effect ¹⁹ | Mild oral irritation, systemic toxicity, allergic reaction ¹⁹ |
| Butyl P-Hydorxybenzoate | 2 (%11,11) | Antimicrobial activity, stabilizer ¹⁸ | Potential endocrine-disrupting effects, may cause irritation or allergic reactions ¹⁸ |
| Calcium Carbonate | 1 (%5,55) | Cleaning, plaque and stain removal ²¹ | Milk-alkali syndrome, allergy or irritation ²¹ |

Table 2. Ingredients in children's Fluoridated Toothpastes (continue)

| Ingredient Type | Occurrence in Flouridated Toothpastes (n) | Function in Toothpaste | Possible Side Effects |
|-----------------------------------|-------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Carbomer | 2 (%11,11) | Stabilizing ingredients, improving spreadability and thickening agent ²² | Mild irritation, allergic reactions, dryness or sensitivity ²² |
| Cellulose Gum | 8 (%44,44) | Viscosity and rheology modifier ²³ | Rare allergies (itching, redness), dry mouth feeling, stomach discomfort ²³ |
| Cinnamal | 1 (%5,55) | Essence, effective against <i>C. Albicans</i> ²⁴ | Mouth irritation (burning, tingling), contact dermatitis ²⁵ |
| CCP-ACP | 2 (%11,11) | Remineralize enamel, cariostatic effect ²⁶ | Milk allergy concern, mild irritation ²⁶ |
| CMC-Na | 2 (%11,11) | Thickener and stabilizer ²⁷ | Skin and digestive irritations ²³ |
| CI 16035 | 3 (%16,66) | Synthetic colorant ²⁸ | Allergic reactions, hyperactivity risk ²⁸ |
| CI 16185 | 1 (%5,55) | Synthetic colorant ²⁶ | No specific side effects listed |
| CI 16255 | 1 (%5,55) | Synthetic colorant ²² | Mild allergic reactions ²⁶ |
| CI 17200 | 1 (%5,55) | Synthetic colorant ²⁸ | No specific side effects listed |
| CI 77019 | 1 (%5,55) | Pearlescent pigment ²⁸ | Minor skin or lung irritation ²⁶ |
| CI 42090 | 1 (%5,55) | Synthetic colorant ²⁸ | Rare allergic reactions ²³ |
| CI 77891 | 2 (%11,11) | Opacifying agent ²⁷ | Mild irritation, inhalation concerns ²⁸ |
| CI 77491 | 1 (%5,55) | Pigment colorant ²⁷ | No specific side effects listed ²² |
| Citric acid | 2 (%11,11) | Prevents dry mouth ²⁹ | Halitosis, demineralization, dentin hypersensitivity, burning mouth syndrome ³⁰ |
| Cocamidopropyl Betaine | 7 (%38,88) | Surfactant ²⁹ | Irritation ²⁹ |
| Ethyl p-hydroxybenzoat | 2 (%11,11) | Preseervative ²⁹ | Rare allergies ²⁹ |
| Decyl Glucoside | 1 (%5,55) | Cleanser ²⁹ | No specific side effects listed |
| D-sorbitol | 2 (%11,11) | Humectant ²⁹ | No specific side effects listed |
| Disodium Cocoyl Glutamate | 1 (%5,55) | Surfactant, cleanser ³¹ | Mild irritant, moisturizing ³¹ |
| Glucose Oxidase | 1 (%5,55) | Antibacterial agent, preservative ³² | Skin irritation and allergic reactions ³² |
| Glucoside | 2 (%11,11) | Non-ionic surfactant ³³ | Mild irritation ³³ |
| Glyceryl Caprylate | 1 (%5,55) | Emulsifier ³⁴ | Rare allergic reactions ³⁴ |
| Glycerin | 10 (%55,55) | Humectant ³² | Toxic effect on kidney and liver ³⁵ |
| Guar gum | 2 (%11,11) | Thickening agent ³⁵ | No specific side effects listed |
| Hydrated Silica | 12 (%66,66) | Abrasive ²⁹ | Gastrointestinal irritation ²⁹ |
| Hydrogenated Starch Hydrolysate | 4 (%22,22) | Humectant, sweetener ³⁶ | Mild digestive issues ³⁶ |
| Hydroxy Ethyl Cellulose | 3 (%16,66) | Thickener, stabilizer ³⁷ | Rare skin irritation ³⁷ |
| Lauryl Glucoside | 2 (%11,11) | Gentle cleansing ³⁸ | Skin or eye irritation ³⁸ |
| Limonene | 2 (%11,11) | Antibacterial properties ³⁹ | Rare allergic reactions ³⁹ |
| Magnolia Officinalis Bark Extract | 1 (%5,55) | Antibacterial, antioxidant ⁴⁰ | Skin irritation ⁴⁰ |

Table 2. Ingredients in children's Fluoridated Toothpastes (continue)

| Ingredient Type | Occurrence in Flouridated Toothpastes (n) | Function in Toothpaste | Possible Side Effects |
|--------------------------------|-------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------|
| Magnesium Oxide | 2 (%11,11) | Abrasive, pH adjuster ⁴¹ | Mild irritation ⁴¹ |
| Metylparaben | 3 (%16,66) | Prevents microbial growth ⁴² | Affects the endocrine system by acting estrogen-like ⁴² |
| Nicotinyl Alcohol HF | 2 (%11,11) | Vasodilator ⁴³ | Skin flushing and mild irritation ⁴³ |
| PEG-6 | 1 (%5,55) | Emulsifier, solubilizer ⁴⁴ | No study in the literature |
| PEG-12 Allyl Ether | 6 (%33,33) | Surfactant ⁴⁵ | Mild skin irritation ⁴⁵ |
| PEG-12 Dimethicone | 7 (%38,88) | Emollient, conditioning agent ⁴⁶ | No study in the literature |
| PEG 600 | 1 (%5,55) | Humectant, solubilizer ⁴⁷ | No study in the literature |
| Pentylene Glycol | 1 (%5,55) | Humectant, antimicrobial stabilizer ⁴⁸ | Rare allergic reactions ⁴⁸ |
| Phosphoric Acid | 2 (%11,11) | pH adjuster, tartar control agent ⁴⁹ | Corrosive to tooth enamel and irritant ⁴⁹ |
| Polylysine | 1 (%5,55) | Antimicrobial agent, preservative ⁵⁰ | Skin irritation ⁵⁰ |
| Polysorbate-20 | 3 (16,66) | Solvent ⁵¹ | Irritant to epithelial cells in the digestive system ⁵¹ |
| Polysorbate-80 | 2 (%11,11) | Solvent ⁵¹ | Irritant to epithelial cells in the digestive system ⁵¹ |
| Potassium Hydroxide | 3 (%16,66) | pH adjuster, solvent ⁵¹ | Irritant, corrosive ^{50,51} |
| Potassium Sorbate | 3 (%16,66) | Antimicrobial effect ⁵² | Mild skin irritation and allergic reactions ⁵² |
| Proplene Glycol | 2 (%11,11) | Solvent ⁵³ | Skin irritation, allergic contact dermatitis ⁵³ |
| Propyl Gallate | 1 (%5,55) | Antioxidant, preservative ⁵⁴ | Allergic reactions ⁵⁴ |
| Propyl P-Hydroxybenzoate | 9 (%49,95) | Inhibiting bacterial and fungal growth ⁵⁵ | Potential endocrine disruptor ⁵⁵ |
| Silica | 3 (%16,66) | Abrasive ²⁹ | Gastrointestinal irritation ²⁹ |
| Silicon Dioxide | 2 (%11,11) | Abrasive, anti-caking agent ⁵⁶ | Lung irritation ⁵⁶ |
| Stevia Rebaudiana Extract | 2 (%11,11) | Sweetener, antioxidant properties ⁵⁷ | Bloating, mild digestive issues ⁵⁷ |
| Steviol Glycosides | 1 (%5,55) | Sweetener ⁵⁸ | No specific side effects listed |
| Sodium Benzoate | 8 (%44,44) | Foaming, anti-staining activity and Anti-gingivitis effect ⁵⁹ | Cytotoxic effect of human gingival fibroblasts ⁶³ |
| Sodium Carboxymethyl Cellulose | 1 (%5,55) | Thickener, stabilizer ⁶¹ | No specific side effects listed |
| Sodium Chloride | 1 (%5,55) | Thickener, flavor enhancer ⁶² | Dryness or irritation ⁶¹ |
| Sodium Fluoride | 15 (%83,34) | Cariostatic activity ¹⁶ | Skeletal, dental and some systemic problems ¹⁵ |
| Sodium Propionate | 3 (%16,66) | Preservative, antifungal agent ⁶⁴ | Mild irritation ⁶⁴ |
| Sodium Saccharin | 11 (%61,11) | Sweetener ⁶⁵ | Carcinogenic, allergen ⁶⁵ |

Table 2. Ingredients in children's Fluoridated Toothpastes (continue)

| Ingredient Type | Occurrence in Fluoridated Toothpastes (n) | Function in Toothpaste | Possible Side Effects |
|-----------------------------|-------------------------------------------|-----------------------------------------------------|---------------------------------------------------------------------|
| Sodium lauryl Sarconsinate | 3 (%16,66) | Surfactant, foaming agent ⁶⁶ | Mild skin and mucosal irritation ⁶⁶ |
| Sodium lauryl sulphate | 1 (%5,55) | Surfactant ⁶⁷ | Toxic effect on oral cells ⁶⁷ |
| Sodium Metyl Cocoyl Taurate | 1 (%5,55) | Surfactant, foaming agent ⁶⁸ | No specific side effects listed |
| Sorbitol | 8 (%44,44) | Sweetener ⁶⁹ | No specific side effects listed |
| Sucralose | 1 (%5,55) | Sweetener ⁷⁰ | Alter gut microbiota with excessive consumption ⁷⁰ |
| Tetrasodium Pyrophosphate | 1 (%5,55) | Tartar control ⁷¹ | Mild mucosal irritant ⁷¹ |
| Tetrasodium EDTA | 3 (%16,66) | Chelating agent ⁷² | Skin irritation, rare allergic reactions ⁷² |
| Titanium dioxide | 5 (%27,77) | Whitening agent, colorant ⁷³ | Potential toxicity with prolonged use ⁷³ |
| Trisodium Phosphate | 2 (%11,11) | pH adjuster, cleansing agent ⁷⁴ | Irritating to gums and oral tissues ⁷⁴ |
| Xanthan gum | 3 (%16,66) | Thickening agent, Stabilizer ⁷⁵ | Mild digestive discomfort if ingested in high amounts ⁷⁵ |
| Xylitol | 8 (%44,44) | Sweetener, anti-cavity agent ⁷⁶ | Bloating or diarrhea in excessive amounts ⁷⁶ |
| Zinc Oxide | 2 (%11,11) | Antibacterial, remineralization agent ⁷⁷ | Irritation ⁷⁷ |

As indicated in Table 2, fluoride compounds (Sodium Fluoride - 83.34%, Amine Fluoride - 16.66%) were the primary active agents responsible for cavity prevention.^{80,81} However, only 9.78% of the analyzed toothpastes contained the EAPD-recommended 1000 ppm fluoride concentration, with another 9.78% falling below the optimal threshold (500-990 ppm F).⁸² The overwhelming availability of fluoride-free toothpastes (80.44%) may potentially influence parents toward choosing 'natural' alternatives, possibly due to concerns over fluoride toxicity or marketing practices. However, this observation is based on product availability and does not directly reflect consumer purchasing behavior.^{83,84} This imbalance could contribute to an increased risk of early childhood caries (ECC), particularly in children without access to fluoride from other sources (e.g., drinking water or professional treatments).⁸⁵

Beyond fluoride, the widespread use of abrasives (Hydrated Silica - 66.66%, Calcium Carbonate - 5.55%) highlights a strong emphasis on mechanical plaque removal.⁸⁶ While these ingredients are effective for stain and plaque control, excessive abrasiveness may pose risks for enamel erosion in young children.^{87,88} Furthermore, preservatives and stabilizers were heavily

represented, with Sodium Benzoate (44.44%) and Propyl P-Hydroxybenzoate (49.95%) being among the most frequently used.^{89,90} Table 1 highlights concerns regarding Sodium Benzoate's cytotoxicity to human gingival fibroblasts, while paraben derivatives like Propyl P-Hydroxybenzoate may act as endocrine disruptors.^{91,92} Additionally, foaming agents such as Sodium Lauryl Sulfate (5.55%) and PEG-based surfactants were common, yet some of these compounds are known mucosal irritants and have potential toxicity concerns in long-term exposure.^{93,94} The presence of Titanium Dioxide (27.77%), widely used for toothpaste whitening, further introduces concerns related to potential nanoparticle absorption and systemic toxicity risks.^{95,96} Given the diverse and complex formulation of fluoridated toothpaste products, these findings emphasize the need for improved consumer awareness, regulatory oversight, and market interventions to ensure safe and effective pediatric oral care options.⁹⁷ While fluoride remains the most scientifically validated anti-caries ingredient, its low availability in the market suggests a disconnect between clinical recommendations and parental purchasing behaviors.⁹⁸ To bridge this gap, future efforts should focus on increasing fluoride toothpaste accessibility, ensuring formulations minimize

potentially harmful preservatives and irritants, and educating parents on evidence-based oral health practices.^{99,100}

DISCUSSION

Fluoride-containing children's toothpastes are widely recommended for their anti-caries benefits, yet concerns remain regarding their potential toxicity, systemic effects, and ingredient safety. In this study, we identified a total of 146 distinct ingredients in fluoride-containing children's toothpastes, some of which have documented toxicological risks (Table 1). While fluoride remains the primary cariostatic agent, excessive exposure in young children has been associated with dental fluorosis and potential systemic toxicity.¹⁰¹ Furthermore, there is growing concern about the cumulative systemic burden of chronic fluoride exposure, especially considering multiple sources such as drinking water, dietary intake, and dental products.^{101,107}

In this study, only fluoride-containing children's toothpaste products underwent detailed compositional analysis. This decision was based on current evidence-based guidelines issued by major pediatric dental associations, including the European Academy of Paediatric Dentistry (EAPD), Australian Research Centre for Population Oral Health (ARCPH) which advocate the use of fluoride-containing toothpaste for effective caries prevention in children.^{7,14} Fluoride-free toothpaste formulations, although available in the market, were excluded from detailed analysis due to their lack of established caries-preventive efficacy.

One of the major concerns regarding fluoride use in pediatric oral care is the risk of ingestion, especially in children aged 0-6 years, who have a higher tendency to swallow toothpaste during brushing.¹⁰² If ingested in excessive amounts, fluoride can accumulate in bones and soft tissues, potentially leading to skeletal fluorosis or neurotoxic effects.¹⁰³ This raises the question of whether fluoride-free remineralization alternatives, such as hydroxyapatite and calcium phosphate, could provide a safer yet effective alternative to traditional fluoride formulations.¹⁰⁴ Although current fluoride safety thresholds are primarily based on skeletal outcomes, emerging studies suggest that neurodevelopmental risks may arise at lower exposure levels than previously recognized.¹⁰²⁻¹⁰⁴

Beyond fluoride toxicity, several commonly used excipients in these toothpastes also pose potential health risks. Our study found that 44.44% of the analyzed fluoridated products contained Sodium Benzoate, a preservative with cytotoxic effects on human gingival fibroblasts, which may compromise oral tissue health with prolonged exposure. Sodium Benzoate has been demonstrated to induce oxidative stress and mitochondrial dysfunction in oral cell

cultures, suggesting that chronic exposure may impair tissue repair mechanisms.¹⁰⁵ Similarly, Sodium Lauryl Sulfate (SLS), identified in 5.55% of the samples, is a known mucosal irritant, linked to increased prevalence of aphthous ulcers.¹⁰⁶ Additionally, Titanium Dioxide (27.77%), frequently used as a whitening agent, has raised concerns regarding potential nanoparticle absorption and carcinogenicity in recent toxicological studies. Particularly concerning is the increasing evidence that nano-sized Titanium Dioxide particles may translocate across mucosal barriers and accumulate systemically, raising concerns over cumulative toxic effects in children.¹⁰⁷

In addition to fluorosis, emerging research suggests that excessive fluoride exposure may have neurotoxic effects, particularly in developing children. Several epidemiological studies have reported an inverse relationship between high fluoride intake and cognitive function, raising concerns about fluoride's potential impact on neurodevelopment.¹⁰⁸ While the majority of fluoride toxicity research has focused on skeletal effects, the possible neurodevelopmental consequences warrant further investigation. This is particularly important for young children, as their developing nervous system may be more vulnerable to fluoride accumulation.¹⁰⁹ Current regulatory standards focus primarily on dental health outcomes, yet there is a need to incorporate neurotoxicological evaluations into fluoride safety assessments.

An alternative approach to fluoride-based caries prevention is the incorporation of biocompatible remineralization agents, such as hydroxyapatite, calcium phosphates, and bioactive glass.¹¹⁰ While these compounds have been studied for their ability to promote enamel remineralization, their long-term efficacy compared to fluoride remains inconclusive. However, hydroxyapatite has demonstrated promising results in reducing demineralization, repairing early carious lesions, and providing an antimicrobial effect without systemic toxicity risks. For instance, randomized clinical trials have demonstrated that nano-hydroxyapatite toothpaste can achieve remineralization rates comparable to fluoride toothpaste in early enamel lesions, offering a potentially safer alternative for young children.¹¹¹ If fluoride toxicity concerns continue to grow, the development of fluoride-free yet equally effective remineralization strategies could redefine pediatric oral care standards. Further clinical research is needed to evaluate whether hydroxyapatite and other biomimetic alternatives can serve as a safer substitute for fluoride in children's oral hygiene products.

Several ingredients commonly found in children's fluoridated toothpastes, such as Sodium Benzoate and Titanium Dioxide, have been associated with potential cytotoxic or systemic effects. Additionally, although polyethylene glycol (PEG) compounds are generally

regarded as safe in cosmetic products, specific toxicological studies are limited, and further research is warranted to fully evaluate their long-term safety in pediatric oral care products.^{44,45} Although some types of PEG (such as PEG/PPG-17/6, PEG-40, and PEG-60) have been reported to have low levels of toxicity. However, PEG products are generally considered safe for use in cosmetic and personal care products. Specific studies are needed for further evaluation.⁷⁸ These findings highlight the necessity for more rigorous safety evaluations of non-fluoride excipients used in children's toothpaste formulations.

Our study's strength lies in its comprehensive evaluation of the fluoride-containing children's toothpaste products available within the Turkish market, offering valuable baseline data in a region where limited national surveys exist. Nevertheless, limitations must be acknowledged. Firstly, we did not evaluate the purchasing patterns or consumer behaviors associated with these products. Thus, our observations regarding potential parental misconceptions about fluoride are inferential and should be interpreted cautiously. Secondly, detailed compositional analysis was restricted to fluoride-containing formulations, excluding fluoride-free alternatives, which may offer additional insights regarding excipient safety profiles.

Future research should prioritize multi-faceted approaches: integrating chemical analysis with consumer behavior studies, investigating parental knowledge and perceptions of fluoride, and evaluating the clinical efficacy of both fluoride-based and fluoride-free remineralization strategies. Additionally, there is a pressing need for comprehensive toxicological assessments of all non-fluoride excipients commonly used in pediatric toothpaste formulations to ensure their biocompatibility and long-term safety.

In conclusion, while fluoride remains the gold standard for caries prevention, balancing its proven efficacy with emerging toxicity concerns is critical. Regulatory bodies should not only enforce optimal fluoride concentrations but also demand transparency and safety evaluations for auxiliary ingredients in pediatric oral care products. A coordinated effort among clinicians, researchers, regulatory agencies, and the industry is necessary to develop safer, evidence-based pediatric toothpaste formulations that align with evolving public health priorities.

CONCLUSIONS

This study highlights critical concerns regarding fluoride exposure, ingredient safety, and market trends in pediatric toothpaste formulations. The limited availability of fluoride-containing children's toothpaste products in Turkey may indicate a potential disconnect

between clinical recommendations and the marketing trends influencing parental choices. However, further research including purchasing data would be necessary to confirm this hypothesis. The dominance of fluoride-free formulations (80.44%), despite EAPD recommendations for 1000 ppm fluoride-containing toothpaste, raises concerns about the effectiveness of marketed oral care products in preventing early childhood caries (ECC).

Beyond fluoride accessibility, this study also sheds light on potential health risks associated with commonly used excipients in fluoridated toothpaste products. The presence of Sodium Benzoate (44.44%), a known cytotoxic agent, along with Sodium Lauryl Sulfate (5.55%), a well-documented mucosal irritant, underscores the need for enhanced regulatory oversight on ingredient safety. Additionally, Titanium Dioxide (27.77%), frequently used as a whitening agent, has been flagged for its potential toxicity and nanoparticle absorption concerns, highlighting the necessity for further toxicological evaluations.

While fluoride plays an essential role in cavity prevention, increasing research suggests that excessive fluoride intake, particularly through accidental ingestion in children, may lead to systemic toxicity, neurodevelopmental concerns, and fluorosis. These findings align with emerging epidemiological evidence pointing to potential cognitive and developmental risks associated with high fluoride exposure. Given these concerns, future research should focus on identifying safer remineralization alternatives, such as hydroxyapatite and calcium phosphate-based.

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