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*Review article*

# A Short Review of Harmful Ingredients in Toothpastes and Their Health Effects

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**Abstract**
Various microbial communities affect the progression of gingivitis and periodontitis, with more than 700 microbial species located within the oral cavity. Toothpaste is an abrasive-based product present in different forms, such as a paste, gel, foam, or liquid, containing both active and non-active ingredients. It plays a role in oral health, prevention of dental decay, and maintenance of oral hygiene through its anti-plaque and antimicrobial properties. Although toothpastes exhibit health-beneficial properties, the majority of toothpastes' compositions contain specific ingredients that can cause adverse effects or cytotoxic responses as a result of misuse, or some individuals are allergic to certain ingredients. Due to the rapid increase in the market for toothpastes, it is essential to evaluate the chemical composition and advantages or disadvantages of oral hygiene products. This article addresses recent data about harmful toothpaste ingredients and their impact on oral and body health.
**Keywords.** Harmful Toothpaste Ingredients, Adverse Effects, Oral and Body Response

## Introduction

According to the U.S. Food and Drug Administration (FDA), toothpaste is an abrasive-based product present in different forms, such as a paste, gel, foam, or liquid, containing both active and inactive ingredients. The process of natural dental plaque removal, improving tooth aesthetics, and maintaining good oral hygiene can be performed by using this product with a toothbrush. The mechanism of tooth brushing depends on the application of a slight force to the tooth surface over a period of time and determines dental plaque removal and the assistance of the active ingredients within the toothpaste.[1]. In general, out of 185 different formulations, more than 20 ingredients are included in current toothpaste formulations [2]. Typically, the main composition of toothpastes is dependent on three primary elements including fluorides, abrasives, and detergents. [3]. Regardless of its interaction with hard tooth structures, both gingiva and mucosal tissues are also susceptible to the action of toothpaste. After application, these products may persist in the oral cavity for many hours, where the concentration of active ingredients within the oral mucosa is higher than in saliva[4]. Because people of all age groups are exposed to toothpaste ingredients through daily use or swallowing it by accident during brushing, periodic assessment of the product is crucial [5]. Even though these products are usually safe, Individuals are regularly subjected to various household items, including shampoo, soap, and toothpaste; the risks of accidental swallowing of these goods must be assessed[6].

Despite the beneficial properties of toothpaste, certain ingredients can cause adverse effects due to individual sensitivities or improper use. Almost all toothpaste formulations contain components that may cause cytotoxic and/or allergic responses in some individuals[2]. Several studies have demonstrated side effects that may arise from some toothpaste ingredients, including oral mucosal irritation and desquamation, resulting in conditions including "stomatitis", "glossitis", "gingivitis", and "buccal mucositis". Furthermore, these ingredients may also give rise to adverse physical effects, such as allergic or toxic reactions[7]. – toothpaste selection should be based on effectiveness, intended purposes, and potential health effects to prevent any undesirable effects[8]. This review discusses the effect of toothpaste ingredients on oral and body health. Although they are safe when used as directed, excessive intake of certain ingredients may lead to significant health risks.

### *Review of Common Cytotoxic Toothpaste Ingredients and Their Effect on Oral and Bodily Health*

Toothpaste formulations differ from one brand to another. In general, ingredients are classified as either active or inactive. Active ingredients include anti-caries, desensitizing, and antimicrobial agents, and the inactive ingredients are composed of abrasives, detergents, humectants, thickening agents, and flavoring agents[4]. Additionally, certain additives in toothpastes can cause toxicity and harmful effects on the oral mucosa, oral bacteria, and systemic health if ingested in sufficient amounts or by accident. These additives include:

### *A-Active ingredients*

### *Fluorides (anti-caries)*

Fluoride plays the most important role as the most significant element in toothpaste. It reduces the occurrence of dental caries and strengthens teeth by encouraging fluoroapatite formation. [9, 10]. Topical fluoride is available in various forms, such as toothpastes, gels, foams, varnishes, and mouthwashes. [11]. It has been widely adopted because of its antibacterial and anti-caries properties[12]. In most cases, the fluoride content in most fluoridated toothpastes typically ranges from 1,000–1,100 ppm. Most fluoridated toothpastes contain approximately 1,000–1,100 ppm of fluoride. With a fluoride concentration ranging from 1.0 to 1.5 mg of fluoride per gram, a 0.5 g dose taken by children aged 2 to 5 years would correspond to an intake of approximately 0.50 to 0.75 mg of fluoride per brushing[13]. Over time, a range of fluoride-based compounds have been incorporated, including “stannous fluoride (SnF2)”, “sodium fluoride (NaF)”,


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"sodium mono-fluoro-phosphate (SMFP)", "acidulated phosphate fluoride (APF)", and "amine fluoride (AmF)". Stannous fluoride has been added as a multifunctional active ingredient due to its broad-spectrum antimicrobial activity. Previous investigations indicate that stannous fluoride inhibits dental plaque activity, demonstrating greater efficacy than many alternative compounds [14]. Recent scientific studies indicate that stannous fluoride possesses multifaceted beneficial properties, including prevention of mineral loss within tooth structure, reduction of dental plaque stability, alleviation of dental hypersensitivity, and promotion of healthier gums. Under controlled usage conditions, fluoride is considered a safe and effective ingredient with demonstrated safety and efficacy for daily oral hygiene, making it appropriate for use by all ages. In recent years, its inclusion in toothpaste has undergone rigorous scientific examination, given concerns regarding the potential for adverse effects in the event of misuse[15]. In comparison to other fluoridated non-stannous agents, SnF2 demonstrated greater efficacy than sodium fluoride or sodium monofluorophosphate [16]. Amalunweze *et al* and Prete *et al* showed that Fluoridated toothpaste is not recommended before the sixth year of age, given that it may cause discoloration of teeth, mouth, tongue, taste alterations, irritation, oral dryness, gingival desquamation, and other adverse systemic effects associated with excessive ingestion or prolonged use[17, 18]. It is hypothesized that chronic daily intake of fluoride from water, food, or dental products at concentrations exceeding 1 mg/L or 0.1 mg/kg during tooth development can induce dental fluorosis. Clinically, this presents as mild opaque white or brown enamel spot lesions on both primary and permanent teeth[19]. While sodium fluoride is the simplest form of fluoride and is an essential element found in most toothpastes.[20, 21]. Excessive intake or prolonged use of fluoride can also cause skeletal fluorosis and potential neurological disturbances[6]. Estimated acute doses range from 1-10 mg/kg. Initial clinical symptoms of acute oral fluoride intoxication in humans include intense nausea, vomiting, hyper salivation, abdominal pain, and diarrhea. In severe or fatal cases, progression to convulsions, cardiac arrhythmias, and eventual coma has been reported. While doses exceeding 15 to 30 mg/kg are considered potentially fatal[13]. Dental professionals, parents, and caregivers must be well informed about the potential complications of excessive fluoride intake to ensure safe oral hygiene practices for all age groups.

***Antiplaque/Anti- gingivitis Agents***

***Zinc***

Through antibacterial action, zinc in oral hygiene products attacks dental plaque bacteria, reduces bad breath by inhibiting volatile sulfur compounds, and prevents tartar deposition by altering crystal growth patterns. Various salt forms of zinc are incorporated by manufacturers, including: oxide, citrate, chloride, lactate, and sulphate [22, 23]. In oral care product formulation, manufacturers frequently incorporate various zinc forms with other active ingredients like fluoride to enhance their therapeutic efficacy. According to the Scientific Committee on Consumer Safety, water-soluble zinc salts "Zinc oxide, Zinc citrate and Zinc chloride" are safe for toothpaste use in children and adults aged 0.5 to 17 years [10].

***Triclosan***

Although Triclosan (2'-hydroxy-2,4,4'-trichlorodiphenyl ether) is used as a potent broad-spectrum antibacterial agent in various personal care and household products, particularly toothpaste at a concentration of approximately 0.3% w/w (compared to 2% w/w for Gantrez). Toxicological investigations indicated that short-term, low-dose exposure in murine models causes gut pathology. Observed symptoms included mild colonic inflammation and increased prevalence of colitis and a higher incidence of colitis-related colonic carcinoma. According to Liu et al. (2022) and Yang et al. (2018), the adverse findings of the pro-colitic and pro-neoplastic effects in animal studies might indicate a health risk to humans, who are repeatedly exposed to triclosan through daily hygiene routines. [24]. Conversely, a five-year follow-up study of patients with cardiovascular disease reported that the persistent use of triclosan-containing toothpaste was associated with a slower progression of periodontitis. Other research has indicated that triclosan may function as an endocrine-disrupting chemical in various species, including humans [25]. Also, evidence indicates that triclosan inhibits cellular synthesis of certain inflammatory cytokines and mediators by human gingival fibroblasts[13].

***Chlorhexidine***

Chlorhexidine is an oral antiseptic that effectively removes dental plaque, which lowers the incidence of dental caries and may help prevent gingivitis and periodontitis. However, studies have shown that long-term exposure to chlorhexidine may trigger anaphylactic reactions and various adverse effects, including oral irritation, altered taste sensation, discoloration of teeth, composite restorations, and the tongue, as well as increased calculus deposition. Although rare, prolonged exposure to chlorhexidine may cause serious systemic complications, including ototoxicity, deafness, conjunctivitis, and colitis. [26]. Results from recent in-vitro studies have shown that chlorhexidine can be cytotoxic to human cells, causing both apoptosis (programmed cell death) and necrotic cell death[10]. According to a study by Kotsailidi *et al*., seven studies have documented 20 cases of hypersensitivity reactions within the oral cavity following exposure to oral-hygiene products that contain chlorhexidine, with symptoms including lip swelling, superficial mucosal necrosis with white desquamative patches, ulcers, and vesicles, associated with pain or a burning sensation. The onset of symptoms may begin a few hours after using toothpaste, but can also be delayed to several days or even weeks, depending on the susceptibility of individuals and the severity of exposure [27, 28].


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***Abrasives***

Abrasives are white, non-reactive, water-insoluble particles measuring in micrometer size, added to toothpaste to facilitate the mechanical removal of external stains and dental biofilm attached to the tooth pellicle. Despite their cleaning efficacy, their misuse or excessive intake in toothpaste can produce harmful physiological effects. Clinical symptoms associated with excessive use of abrasive-containing toothpastes include: "tooth sensitivity, gingival recession, and dentin hypersensitivity"[29]. Accordingly, it is advisable to avoid, whenever possible, toothpastes that contain abrasive agents as far as possible, particularly for patients who have a high risk of tooth wear, dentinal hypersensitivity(DH), or gingival inflammation [17]. Toothpaste incorporates a variety of widely occurring abrasive ingredients, each characterized by a specific function. Among the most significant harmful constituents the following:

***Calcium carbonate***

Generally, being essential and less toxic than silica, reduces dentin hypersensitivity by occlusion of dentinal tubules. Despite these benefits, high-dose exposure or prolonged topical application of calcium carbonate can be associated with significant systemic effects, such as coronary artery calcification, kidney stone formation, loss of appetite, nausea, and vomiting [30, 31].

***Dicalcium phosphate (CaHPO4)***

Used as an abrasive agent and incorporated into toothpaste as a white powder. Earlier investigations showed that over-consumption of dicalcium phosphate or calcium supplements can cause pathological symptoms that adversely affect systemic health, including: muscle weakness, arrhythmias, confusion, constipation or diarrhea, headaches, fatigue, nausea and vomiting, frequent urination, and—in extreme cases coma [30].

***Hydrous or anhydrous sodium metaphosphate***

Added to water-free toothpaste at concentration approximately 8 % by weight. This water-soluble ingredient plays a significant role in cleaning. Prior results suggest that excessive use of high doses of sodium met phosphates may result in a number of systemic problems like "nausea", "vomiting", "bone pain", "dizziness", and "muscle pain" [30]. The typical concentration of sodium metaphosphate in toothpaste is approximately [2].

***Silica***

Certain whitening and polishing toothpaste formulations incorporate alumina oxides, which appear to be more aggressive toward enamel than silica but demonstrate efficacy for staining removal[30].One study reported an association between toothpaste containing silica and Crohn's disease; silica ingestion from toothpaste has been examined. Although the hypothesis requires further investigation, current scientific evidence remains limited[32].

***Calcium pyrophosphate***

Because calcium pyrophosphate is water-insoluble but acid-soluble, it provides anti-calculus activity. Theoretically, Pyrophosphates may disrupt the equilibrium of demineralization–remineralization processes at the tooth surface; accordingly, toothpastes containing calcium pyrophosphate are not recommended for use in children under 12 years old. [33]. According to Davies *et al*, tartar-control pyrophosphate dentifrices have been associated with adverse reactions including "perioral erythema, scaling, fissuring, cheilitis, gingivitis, and circumoral dermatitis"[34].

***Sodium bicarbonate***

commonly called baking soda, and it is a mild abrasive ingredient that neutralizes acids; however, earlier investigations showed that its inclusion into toothpaste formulations unintentionally reduces the anticariogenic efficacy of fluoride [28].

***Inactive Ingredients***

***Humidifiers/ moisture retainer***

Some humectants like glycerin, sorbitol, propylene glycol, and mannitol are added to toothpaste formulations to prevent moisture loss and maintain consistency. Although they have therapeutic properties, certain humectants have potential side effects. Sorbitol functions as an osmotic laxative, and excessive concentration or long-term exposure can cause diarrhea. According to safety recommendations from the FAO/WHO, the dose of sorbitol should not exceed 150 mg/kg/day. Therefore, parents should closely monitor young children who are using toothpaste gels with high sorbitol concentrations to ensure safety and reduce the chance of side effects [32]. For propylene glycol (PEG), acceptable concentration ranges from 0.5 to 2% by weight; at high concentrations lead to adverse health effects such as irritation and allergic contact dermatitis [2].

***Detergents /foaming agent/Surfactants***

Are essential ingredients in toothpaste formulations, as they are responsible for soap and foam formation and improving toothpaste texture during use. The most common harmful detergents include:


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***Sodium Lauryl Sulfate (SLS)***
SLS is used as a detergent in toothpaste formulations; it reduces surface tension within the oral cavity by improving the foaming action of toothpaste, and it also has Anti-plaque efficacy due to its bacteriostatic properties. Typical concentration ranges from 1-2% in toothpaste formulations. Although it offers these performance advantages, SLS exhibits cytotoxic properties to the oral mucosa, and has been linked to the development of recurrent aphthous ulcers (RAU)[29]. A 1983 American Journal of Toxicology report indicated that low concentrations of SLS, such as 0.5%, can cause irritation, while much higher concentrations, 10% and 30%, may cause severe skin irritation. The authors reported strong skin reactivity, causing swelling and disrupting the stratum corneum. Accordingly, SLS exposure may exacerbate aphthous ulcers, or canker sores, in individuals susceptible to these irritations. Furthermore, systemic absorption of SLS via oral mucosa exhibits estrogen-like activity, resulting in estrogen dysfunction and a variety of health problems from "PMS and Menopausal symptoms to dropping male fertility and increasing female cancers such as breast cancer" [35].

***Cocoamidopropyl betaine (CAPB)***
Is an amphoteric detergent and serves as a substitute for SLS, as CAPB offers more biocompatibility and less mucosal irritation, but it has an unpleasant, bitter taste[36, 37]. CAPB has been reported to induce inflammatory reactions in oral epithelial tissues [4].

***Binders /gelling agent***
The main function of binders is to adjust the product's rheological properties, and their addition is to maintain textural integrity by preventing separation of liquid and powdered ingredients, resulting in homogeneous consistency for the duration of shelf life. Among the most significant binders are: "carrageenan, alginate, sodium carboxymethylcellulose, magnesium aluminum silicate, sodium magnesium silicate and colloidal silica . Necas *et a*l. reported that poor gastrointestinal digestion of carrageenan can result in tumor-like growth and ulceration[38].

***Sweetener***
The most commonly used toothpastes sweeteners utilized are sodium aspartame, saccharin, sodium cyclamate, xylitol, sorbitol, isomalt, and acesulfame-K. Generally, these sweeteners are safe under normal conditions; however, allergic reactions may occur in sensitive individuals. Furthermore, excessive intake of artificial sweeteners can have a laxative effect, resulting in gastrointestinal discomfort. Among these sweeteners, saccharin is a health concern; it is a water-insoluble artificial sugar derived from petroleum, and excessive or long-term exposure has been associated with carcinogenic effects [6, 8]. Ucuncu *et al*. have found that most toothpastes containing saccharin can cause skin allergy and have been linked to cardiac and gastrointestinal issues that threaten systemic health.

***Coloring agents/Pigments***
The main function of coloring agents is to provide opacity and brightness to the toothpaste formulation. The two most harmful pigments are titanium dioxide and calcium carbonate. In the Netherlands, the realistic estimated mean intake of Tio2 by children aged 2-6 years old, through food, dietary supplements, and toothpaste, is about 0.67 mg/kg b w/d. Although this amount appears low, no definitive conclusion has yet been reached about its safety or toxicity [39]. Recent research led by Petrovic et al. raised concerns about TiO2's potential toxicity and its possible classification as a human carcinogen [6, 40]. A study by Ucuncu et al. found that titanium dioxide taken up by children aged (2-6 years) via the oral route was found to be absorbed through the intestines and to cause biological harm at the cellular and molecular levels[8]. Although calcium carbonate is used as an alternative for titanium dioxide, calcium carbonate can interfere with the efficacy of fluoride in toothpaste, mainly with sodium fluoride.

***Flavoring agents***
Oils like peppermint, cinnamon, and spearmint are commonly used to cover the unpleasant taste of the other components of the toothpaste[41]. Certain flavoring agents may induce allergic reactions in some individuals, such as perioral contact dermatitis, stomatitis, or cheilitis, which have been reported as adverse effects[4]. Reynolds *et al*. found that the flavors, colorings, or preservatives in toothpaste formulation can cause allergic responses in some individuals, sometimes presenting as desquamation and swelling of the lips and tongue, perioral dermatitis, angular cheilitis, gingivitis, and intra-oral ulceration. They also observed that certain toothpastes can cause mild irritation of the oral mucosa that subsides immediately after discontinuation, which is attributed to their detergent or essential oil flavor content[32]. Although flavors are added at low concentrations, Lemon, Peppermint, and Cinnamon are known to have irritating effects and are also recognized as sensitizers and may induce an allergic reaction even at low concentrations[2]. Comparable reports show that Menthol and carvone may be associated with dermatological issues, including contact dermatitis[42, 43].

***Preservatives***
Act as preservatives and protective agents. The most significant harmful protective agents that have adverse systemic effects include: Benzoates, paraben, sodium benzoate, and EDTA. Various forms of Paraben (methylparaben, ethylparaben, and propylparaben) may interfere with the endocrine system and exhibit oestrogen-like properties,


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potentially leading to cancer; they may also accumulate in urine and adversely affect urinary tract function. Although sodium benzoate is known for its strong protective properties, research conducted on human gingival fibroblasts has shown cytotoxic and harmful effects of sodium benzoate on cell cultures[8]. Tabatabaei *et al*. investigated the cytotoxicity of sodium benzoate and revealed that this ingredient can cause anaphylactic shock, swelling of the nasal mucosa, and dyspnea[3].

***EDTA***

(ethylene di-amine tetra acetic acid) and formaldehyde are widely used as a preservative agent in commercial toothpaste formulation and numerous other cosmetics and personal care items. It is classified as an environmental pollutant[35].

## Whitening Agents

***Hydrogen Peroxide (H2o2)***

is widely used for tooth whitening and used as a chemical agent to remove superficial discoloration of the teeth. In typical formulations of toothpaste, the effective concentration of H2O2 is approximately 1% w/w. Since this invention emerged, H2O2 has been the subject of extensive investigations due to its possible role in inducing hypersensitivity following treatment. clinical study reported that exposure to high concentrations of H2O2 can be harmful to the organic matrix, thus mechanically weakening the tooth structure[17].

***Charcoal***

As a whitening ingredient in dental care formulations, research has shown that charcoal may be associated with increased surface roughness in enamel. Excessive application of a charcoal-based toothpaste during brushing may cause more harm than benefit, especially to tooth-colored restorations with lower wear resistance[44]. Although charcoal can whiten teeth, it may also adversely affect patients' smiles as charcoal particles can adhere to deposits and stains on the surface of teeth and accumulate within gingival cuffs and pockets, potentially discoloring the brush and darkening the tongue (Greenwall, Greenwall-Cohen, & Wilson, 2019). Investigations by Kowalska *et al*. reported similar results, observing accumulation of charcoal in patients with periodontal disease or deep pockets, which was associated with the appearance of grey or black spots in the gums of affected individuals (Kowalska et al., 2024). Some charcoal-based toothpaste formulations may contain polyaromatic hydrocarbons; these chemical compounds are suspected to be human carcinogenic. Combining bentonite clay in some charcoal-based toothpaste formulations can increase levels of heavy metals. Furthermore, charcoal acts as an absorptive agent that interferes with fluoride efficacy, as fluoride is the main active ingredient in toothpaste to prevent dental caries; this interaction is very undesirable (Valkenburg et al., 2024).

## Additives

***Herbs***

**In** recent years, the incorporation of natural extracts or essential oils into toothpaste formulations has increased. These products exhibit potential antimicrobial activity and lower side effect risks than some chemical ingredients. Medical herbal ingredients that can be added to toothpastes' composition include: sanguinarin extract, propolis, rosary tree, clove (Syzygium aromaticum), aloe vera (Aloe barbadensis), green tea (Camellia sinensis), and miswak (Salvadora persica) tree Plant extracts . While Aloe, curcumin, eucalyptus oil, licorice (Glycyrrhiza glabra), neem (Azadirachta indica), and tea tree oil are widely used in dental care products, particularly toothpastes[10]. Because formulations and concentrations lack standardization, clinical findings differ across studies. Moreover, the potential for interactions between herbal supplements and prescribed medications may induce side effects; therefore, avoid using medical herbals, especially for individuals with health conditions or hypersensitivity reactions[45].

***Licorice***

(Radix glycyrrhizin) is an extract from a medicinal plant used in several applications because of its sweet taste. According to the World Health Organization (WHO), a safe dose or concentration of licorice is 100 mg per day. [46]. Glycyrrhizin has excellent therapeutic benefits in treating various oral diseases, including: "dental caries (anti-cariogenic property), gingivitis, periodontitis, oral candidiasis, recurrent aphthous ulcers and even severe conditions such as oral cancer. Although licorice exhibits these therapeutic properties, it exhibits adverse systemic effects at excessive intake, such as hypokalemia, severe hypertension, metabolic alkalosis, and edemas[47].

***Curcumin***

Curcumin is an extract obtained from the plant Curcuma longa Linn. Researchers suggest that the estimated dose that can be tolerated by humans of curcumin is 12 g/day. Recent investigations and clinical results have found that curcumin has therapeutic properties including anti-inflammatory, antimicrobial, anticariogenic, antioxidant, antifungal, antidepressant properties[10, 48]Despite these health benefits, side effects have been observed in some individuals that require careful attention and medical supervision. Inchingolo *et al*. reported that curcumin has been associated with stains on oral mucosa and enamel surface, especially after long-term use or high doses, which have aesthetic implications that can affect treatment acceptance [49]. Furthermore, Shoba *et al*. reported that exposure to curcumin


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may cause adverse effects and allergic reactions in some individuals, such as facial swelling, difficulty breathing, allergic contact dermatitis and contact urticaria [49, 50].

***Recommendations***

Purchasing decisions for oral hygiene products, particularly toothpastes, should be guided not only by their therapeutic performance and problem-solving effectiveness but also by consideration of potential systemic effects on users. Dental professionals must therefore possess comprehensive knowledge of active ingredients, their clinical indications, and therapeutic concentrations in order to determine the most appropriate toothpaste formulation for each patient. Future investigations are warranted to evaluate the biocompatibility, cytotoxicity, and apoptotic effects of toothpaste formulations through both in vitro and in vivo studies. Such evaluations are especially critical for products prescribed to pediatric patients, individuals with a history of allergies, those susceptible to mucosal hypersensitivity, and patients requiring long-term daily use. Moreover, further research is essential for toothpaste formulations containing herbal products, as these often lack standardized concentrations and uniform formulations. Rigorous scientific evaluation is needed to ensure both their efficacy and safety before widespread clinical recommendation.

## Conclusion

In conclusion, the ideal ingredients in toothpaste formulation should be safe, non-toxic, non-allergenic, and non-irritating to ensure safety and therapeutic efficacy during use. With the rapid expansion of the toothpaste market, dental professionals and consumers should understand the chemical composition and possible advantages and adverse effects of each ingredient before purchasing.

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