

# Green dentistry: Organic toothpaste formulations. A literature review

Marta Mazur<sup>1,A,D</sup>, Artнора Ndokaj<sup>1,B,C</sup>, Sabina Bietolini<sup>2,A,E</sup>, Veronica Nisii<sup>3,A,B</sup>, Irena Duś-Ilnicka<sup>4,B,C</sup>, Livia Ottolenghi<sup>1,E,F</sup>

<sup>1</sup> Department of Oral and Maxillofacial Sciences, Sapienza University of Rome, Italy

<sup>2</sup> Niccolò Cusano University (UNICUSANO), Rome, Italy

<sup>3</sup> Chirurgien Dentiste Centre Publique Mairie de Paris 18ème, Paris, France

<sup>4</sup> Department of Oral Pathology, Wrocław Medical University, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of the article

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## Address for correspondence

Artнора Ndokaj

E-mail: artнора.ndokaj@uniroma1.it

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## Abstract

Dentistry as a profession should take into account the goals of sustainable development in daily practice and encourage the transition to a green economy. Consumers are becoming more conscious about the impact of self-care products, including toothpastes, on the environment. Organic toothpastes are considered very safe. A broad literature review was conducted to: (i) identify the ingredients in available organic toothpastes; (ii) classify them into active and inactive; and (iii) evaluate each ingredient's purpose and the adverse events that may be associated with its use. A comprehensive list of available organic toothpastes and their ingredients was compiled based on the products from the largest Italian organic supermarket chain (NaturaSi®) that is representative of the European market. Then, PubMed, Scopus and Google Scholar databases were searched to identify, classify and evaluate each ingredient. The final sample consisted of 46 organic toothpastes that included 156 ingredients; 139 (89.1%) and 17 (10.9%) were classified as active and inactive, respectively. Overall, 32 (20.5%) ingredients were associated with known adverse events. The results of this study indicate that organic toothpastes are highly biocompatible with oral cavity tissues. Careful product selection may help consumers avoid potential adverse effects that can be caused by ingredients such as polymers (e.g., polyethylene glycol) and carbomers, detergent agents (e.g., sodium lauryl sulfate), and triclosan. The lack of clinical studies should encourage the development of sufficient evidence to provide consumers with recommendations for daily use, based on both efficacy and biocompatibility.

**Keywords:** natural, toxicology, ingredients, organic toothpaste, plant/herbal extracts

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## Introduction

In August 2017, the FDI World Dental Federation published a document titled “Sustainability in Dentistry”<sup>1</sup> that was based on the United Nations “Transforming our world: The 2030 Agenda for Sustainable Development”.<sup>2</sup> It is recommended that dentistry as a profession takes into account the goals of sustainable development in daily practice and encourages the transition to a green economy.<sup>3</sup> Oral health professionals are responsible for reducing their impact on natural resources while promoting optimal oral health for all people and ensuring patient safety.<sup>4</sup> As a result, toothpaste formulations have dramatically improved over the last decade by incorporating safer active ingredients, higher fluoride bioavailability and better stain removal with fewer abrasives.<sup>5</sup> These products are supposed to simultaneously improve many oral diseases and conditions, such as caries, tooth discoloration, hypersensitivity, halitosis, and gingivitis, while also satisfying the expectations of more conscious and demanding consumers.<sup>5</sup>

The development of toothpastes, however, is far from complete. Over the last 20 years, the organic personal care market – of which the oral care subset represents a huge driving force – has grown exponentially and will presumably be nearly doubled by 2022 as compared to 2000.<sup>6</sup>

The requirements to be considered an “organic” product include: (i) the use of substances of natural origin characterized by ecological and skin compatibility and good aquatic toxicity performance; (ii) no genetically modified organisms in either the finished product or its individual ingredients; (iii) the use of natural fragrances (e.g., essential oils); (iv) the use of biodegradable detergents and surfactants; (v) no ionizing radiation; and (vi) the use of natural substances coming from controlled organic farming certified by a recognized accredited independent body.<sup>7</sup>

An attempt has been made to differentiate between active and inactive ingredients in widely marketed non-organic toothpaste formulations.<sup>8</sup> Active ingredients are expected to contribute to improved oral health, while inactive ingredients are added merely to enhance the appeal of the product. Unfortunately, a substantial proportion of inactive ingredients has been associated with adverse events (AEs), including enamel demineralization.<sup>8</sup> A previous review detailing the composition of non-organic toothpaste formulations found that 75.6% of the ingredients were associated with possible AEs.<sup>8</sup> In addition, nearly 30% of the ingredients were inactive.<sup>8</sup> Notably, most individuals were not aware of the risks associated with particular ingredients.<sup>9</sup>

Until now, no data about the content of active and inactive ingredients and the risks associated with organic toothpaste formulations is available in Europe.

Thus, this study aimed to: (i) identify the ingredients in available organic toothpastes; (ii) classify the ingredients into active and inactive; and (iii) evaluate each ingredient’s purpose and the known risks associated with its long-term use.

## Material and methods

### Selection criteria for the organic toothpaste database

The products included in this study were analyzed based on the database from the largest Italian organic supermarket chain, NaturaSi<sup>®</sup>, which has more than 240 shops in the country. They were considered representative of the European market due to the international distribution of most of the products in this field.

We accessed the online database of their dental products (<https://www.naturasi.it/prodotti/cura-della-persona/igiene-orale>) and extracted a list of available toothpastes. As this chain is restricted to organic products, all of the toothpastes surveyed had some European organic certifications. The first coder (MM) compiled the list of ingredients, and the second coder (AN) created a coding sheet to register all the ingredients of each toothpaste.

### Identification of active and inactive ingredients

The authors developed an Excel (Microsoft Corp., Redmond, USA) database that included each ingredient for every selected formulation. Subsequently, each ingredient was classified as active or inactive, according to literature data obtained from PubMed, Scopus and Google Scholar databases from March 2021 to July 2021. In general, active ingredients are considered those typically present in toothpastes, such as emulsifying, buffering, preserving, and wetting agents, as well as thickeners, abrasives, solvents, absorbents, and antibacterial agents. Inactive ingredients include substances such as sweeteners, flavorings, colorants, and fragrance additives.

### Ingredient toxicity

All AEs associated with each ingredient were collected by searching PubMed, Scopus and Google Scholar databases. Adverse events included the following: burning sensation/irritation/swelling/sensitivity of the cheek, tongue, lips, gum, palate, or papillae; tooth sensitivity; peeling/exfoliation/roughness of the cheek, tongue, lips, or gum; presence of aphthous ulcer/wounds; itching/tingling/taste changes of the cheek, tongue or lips; gastrointestinal signs and symptoms; and eye irritation. Since AEs may be individual in nature, the scope of the

analyzed literature included not only randomized controlled trials and case-control studies on human and animal subjects but also case reports.

## Database availability

The supplementary research database associated with this article (Excel database including each ingredient for every selected toothpaste formulation) can be obtained from the corresponding author on reasonable request.

## Results

### Organic toothpaste database

A total of 46 all-natural organic toothpastes sold by NaturaSi® were identified. They were classified according to different countries' certifications; 44 of the 46 toothpastes (95.7%) were marketed in more than 6 European countries. The certificates attesting to the organic nature of the analyzed toothpastes were NATRUE label, Biorganic DE, ICEA Eco Bio Cosmesi, BDIH, AIAB Bio Eco Cosmesi, Cosmebio, Ecocert, and Demeter. The Italian companies included Ecor, Natyr, Bioearth, Ecosi-Pierpaoli s.r.l., Victor Philippe, Lycon Cosmetics, and Argital. The German companies included Sante Naturkosmetik, Lavera Naturkosmetik, Logona Naturkosmetik, and Neobio. There was one product from each of the following countries: Switzerland (Weleda), England (Dr. Hauschka), the Netherlands (Ecodenta), and France (Cattier).

### Identification of overall ingredients

A total of 156 unique ingredients were coded: 139 (89.1%) and 17 (10.9%) ingredients were classified as active and inactive, respectively. Overall, 32 (20.5%) ingredients were associated with known AEs; 23 were in the active group and 9 were in the inactive group.

The calculated mean number of ingredients per toothpaste was  $16.0 \pm 3.8$ . The mean number of ingredients originating from plant extracts was  $6.4 \pm 3.1$ .

Only 8 toothpastes (17.4%) were fluoridated; 6 (13.0%) contained sodium fluoride, and 2 (4.3%) had monofluorophosphate.

A total of 21 (45.7%) formulations contained xylitol, which was always among the first 10 ingredients.

### Identification of active ingredients

One hundred thirty-nine of the 156 ingredients were classified as active. They were subdivided into fluorides, emulsifiers, emollients, buffering agents, wetting agents, preserving agents, thickening agents, abrasives, whitening and plaque removal agents, solvents, absorbents, antibacterials, and active plant/herbal extracts. Among the 139 active ingredients, 23 (16.5%) were reported to have had possible AEs and 82 (59.0%) were organic plant/herbal extract ingredients. According to the literature search for each individual ingredient, none appeared to be related to any AEs.

Table 1 presents the classification of active ingredients according to their purpose and known AEs. Adverse events are listed in the table, when appropriate.

Table 1. Characteristics of the selected studies

Purpose and known adverse events of active toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse events
Active ingredient	sodium fluoride	anti-caries activity, whitening effects, halitosis control <sup>1</sup>	excess ingestion of sodium fluoride was linked with dehydration and with the possibility of dental and skeletal fluorosis <sup>2-4</sup>
	sodium monofluorophosphate	not found	not found
Emulsifiers	sodium lauryl sulfate	thickening and foaming agent <sup>5</sup>	skin, eyes, oral mucosa, and gastrointestinal irritant <sup>6-8</sup>
	sodium carboxymethyl cellulose	emulsion stabilizing agent <sup>9</sup>	no known contamination risks <sup>9</sup>
	poloxamer 407	emulsifying agent <sup>10,11</sup>	eye and renal irritant <sup>12,13</sup> ; in animal studies and with parenteral administration, it was linked to hyperlipidemia and engorgement of Kupffer cells <sup>14</sup>
	tetrasodium pyrophosphate	anti-biofilm action by reducing saliva calcium and magnesium <sup>15,16</sup>	nose, skin, eye, throat, and respiratory tract irritant <sup>17</sup>
	sodium hexametaphosphate	extrinsic stain removal <sup>18</sup>	skin, eye, respiratory tract irritant; can cause gastrointestinal symptoms and lethargy, when ingested <sup>19</sup>
	sodium cocoyl glutamate	surfactant	not found

Purpose and known adverse events of active toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse events
Emulsifiers	disodium cocoyl glutamate	surfactant	not found
	disodium cocoamphodiacetate	surfactant	not found
	algin	thickener	not found
	sodium chloride	moisturizer	not found
	pistacia lentiscus gum	antibacterial activity <sup>20</sup>	not found
	<i>Cyamopsis tetragonoloba</i> (guar) gum	natural thickener	not found
	sodium lauroyl glutamate	surfactant	not found
	lauryl glucoside	foaming agent	allergic dermatitis reported in case studies <sup>21</sup>
	sodium lauroyl sarcosinate	pH buffering agent	non-irritating and non-sensitizing to animal and human skin; can increase the penetration of other ingredients through the skin; low oral toxicity in rats, not mutagenic; no data on carcinogenicity <sup>22</sup>
	betaine	moisturizer and foam stabilizer <sup>23</sup>	not found
	hectorite (natural clay)	excellent absorption capacity <sup>23,24</sup>	not found
magnesium aluminum silicate	excellent absorption capacity	not found	
sucrose laurate	solubilization properties <sup>25</sup>	not found	
Emollients	<i>Triticum vulgare</i> (wheat) germ oil	emollient and antioxidant agent; often mixed with other oils, and used as a base for many creams for mature skin, owing to the high content of tocopherols (vitamin E) which also makes it an excellent antioxidant <sup>23</sup>	not found
	esculin	emollient; glucoside extracted from <i>Aesculus hippocastanum</i> , <i>Aesculus californica</i> and <i>Daphne mezereum</i> <sup>23</sup>	not found
	<i>Helianthus annuus</i> oil (sunflower)	rich in linoleic acid, vitamin E, vitamin A, a powerful antioxidant, helps to maintain the right cholesterol level and protects against cardiovascular diseases by keeping the blood flowing <sup>26,27</sup>	not found
	potassium nitrate	desensitizing agent <sup>28</sup>	not found
Buffering agents	disodium pyrophosphate	remineralizing agent	not found
	sodium hydroxide	buffering agent	unclear toxicity; at high concentrations sodium hydroxide has been shown to affect the viability of esophageal cells <sup>29</sup>
	calcium citrate	remineralizing agent	not found
	sodium silicate	remineralizing agent	extremely toxic in purity to contact <sup>30</sup>
Preserving agents	sodium benzoate	preserving agent	excess consumption could decrease the functioning of the immune system and cause other irritations <sup>31,32</sup>
	potassium sorbate	preserving agent	dangerous in case of ingestion and inhalation; skin and eye irritant <sup>33</sup>
	sodium dehydroacetate	preserving agent	allergic dermatitis reported in case studies <sup>34</sup>
	ethylhexylglycerin	preserving, antibacterial, surfactant, skin-conditioning, emollient agent	a low-risk but relevant sensitizer in 'hypoallergenic' formulations <sup>35</sup>
	salicylic acid	preserving agent	salicylic acid toxicity (salicylism) can occur after topical use of 6% salicylic acid over as little as 40% of body surface area <sup>36</sup>
	sorbic acid	preserving agent	contact urticaria after the use of synthetic cassia oil and sorbic acid limited to the face <sup>37</sup>
Thickening agents	cellulose gum	thickening agent <sup>9</sup>	skin and eye irritant <sup>38</sup>
	xanthan gum	thickening and stabilizing agent <sup>39</sup>	pure xanthan gum could cause bloating, cold and flu-like symptoms <sup>40,41</sup>
	carrageenan	thickening agent <sup>9</sup>	gastrointestinal issues <sup>42-44</sup>

Purpose and known adverse events of active toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse events
Abrasives	calcium carbonate	active in extrinsic stain and plaque removal <sup>45</sup>	eye and respiratory tract irritant <sup>46</sup>
	silica	abrasive agent <sup>47</sup>	not found
	diatomaceous earth (solum diatomeae)	abrasive agent	not found
	illite	abrasive agent	not found
Whitening/plaque removal agents	citric acid	active in dental plaque removal <sup>9</sup>	the developmental toxicity associated with chronic consumption of citric acid is not known <sup>48</sup> ; gastrointestinal symptoms are reported to be associated with citric acid consumption <sup>9</sup>
	hydrated silica	active in extrinsic stain and plaque removal <sup>49</sup>	use of silica nanoparticles in-vivo poses risks of bioaccumulation <sup>50</sup>
	mica	not found	not found
	sodium bicarbonate	active in extrinsic stain and plaque removal <sup>51</sup>	rare reactions such as dizziness, confusion, irritability, memory problems, muscle pain or aches, vomiting, or weakness are reported to be associated with its excess consumption <sup>52</sup>
	titanium dioxide	active in extrinsic stain removal <sup>53</sup>	mixed findings; recent work suggested that titanium dioxide in higher concentrations may be dangerous <sup>53</sup> ; particularly, chronic health effects include possible harm to the upper respiratory tract and lungs <sup>54</sup>
	trisodium phosphate	not found	not found
Wetting agents	xylitol	active in caries prevention <sup>55</sup>	no carcinogenicity <sup>55</sup>
	glycerin	used to prevent toothpaste from drying out <sup>56</sup>	generally used with low toxicity, but at high concentrations, it could impair blood circulation <sup>57</sup>
	hydrogenated starch hydrolysate	used also as a sweetener (polyol (sugar alcohol))	not found
	lactose	used also as a sweetener	not found
Solvents	calcium lactate	used also as an enamel remineralizer	not found
	aqua	solvent	not found
	denatured alcohol	solvent	not found
Absorbents	alcohol	solvent	not found
	kaolin	cleaning and polishing agent	not found
	solum fullonum	absorbent	not found
	maltodextrin	used also as a sweetener	not found
Antibacterials	charcoal powder	buffering agent	not found
	<i>Copaifera officinalis</i> resin	antibacterial agent	not found
	honey (Manuka honey IAA15+)	antibacterial agent	not found
	<i>Anthemis nobilis</i> extract (chamomile)	antibacterial, antifungal, insecticidal, hypotensive, anti-platelet aggregation, anti-inflammatory, hypoglycemic, and antioxidant agent <sup>58</sup>	the US Food And Drug Administration (FDA) classified the oil and extract of Roman chamomiles as safe <sup>58</sup>
	bisabolol	antibacterial and thickening agent	not found
Other ingredients	carvone	antibacterial agent	not found
	Aloe vera	antioxidant and antibacterial properties	not found
Vegetable-based ingredients	<i>Mentha arvensis</i> oil	analgesic counterirritant	not found
	<i>Mentha arvensis</i> flower/leaf/stem extract	analgesic counterirritant	sensitizer; case reports on allergic contact cheilitis caused by toothpaste menthol <sup>59</sup>
	<i>Mentha viridis</i> (spearmint) leaf oil	analgesic counterirritant	sensitizer and allergenic <sup>59</sup>
	<i>Melissa officinalis</i> flower/leaf/stem water	antimicrobial and antioxidant agent	case reports on contact dermatitis <sup>60</sup>
	<i>Aloe barbadensis</i> leaf juice	emollient and antimicrobial agent; used to treat aphthous ulcers and to reduce the incidence of alveolar osteitis after third molar extraction surgeries <sup>61</sup> ; a mouthrinse containing <i>A. vera</i> was found to reduce gingival inflammation and gingival bleeding <sup>62</sup> and was more effective than Listerine® in reducing the count of aerobic, microaerophilic and anaerobic bacteria <sup>63</sup>	not found

Purpose and known adverse events of active toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse events
	<i>Aloe barbadensis</i> gel	emollient, antimicrobial	not found
	<i>Mentha piperita</i> oil	analgesic, antiseptic and anti-inflammatory properties <sup>64</sup>	not found
	<i>Myrtus communis</i> leaf water	antibacterial activity on oral pathogens: <i>Streptococcus mutans</i> , <i>Aggregatibacter actinomycetemcomitans</i> , <i>Porphyromonas gingivalis</i> , <i>Streptococcus pyogenes</i> and <i>Candida albicans</i> <sup>65</sup>	not found
	<i>Echinacea purpurea</i> extract	immunostimulant, increases interferon production <sup>66</sup>	not found
	<i>Salvia officinalis</i> (sage) leaf extract	antioxidant	not found
	<i>Salvia officinalis</i> oil	antioxidant	not found
	<i>Salvia sclarea</i> (clary) oil	antioxidant	not found
	<i>Salvia triloba</i> (sage) leaf oil	antioxidant	not found
	<i>Mentha piperita</i> (peppermint) leaf extract	analgesic counterirritant	not found
	<i>Glycyrrhiza glabra</i> root extract	anti-inflammatory activity	not found
	<i>Camellia sinensis</i> leaf water	antimicrobial	not found
	<i>Camellia oleifera</i> leaf extract	antimicrobial	not found
	<i>Mentha spicata</i> herb oil	analgesic counterirritant	not found
	<i>Krameria triandra</i> extract	astringent	not found
	<i>Elettaria cardamomum</i> seed oil	active on oral cavity disinfection and halitosis; regulates inflammatory and immune function <sup>67</sup>	not found
	<i>Citrus limon</i> peel oil	antibacterial agent	not found
	<i>Achillea millefolium</i> extract	hydrating agent	not found
	<i>Echinacea angustifolia</i> root extract	immunostimulant agent: increases interferon production	not found
Vegetable-based ingredients	<i>Echinacea pallida</i> extract	immunostimulant agent: increases interferon production	not found
	<i>Arnica montana</i> flower extract	antimicrobial, anti-inflammatory, antibiotic and antifungal agent	not found
	<i>Melaleuca alternifolia</i> leaf oil	antimicrobial agent	not found
	<i>Fragaria chiloensis</i> fruit extract	astringent effect	not found
	<i>Rubus idaeus</i> fruit extract	anti-biofilm formation	not found
	<i>Rosmarinus officinalis</i> (rosemary) leaf extract	anti-biofilm formation	not found
	<i>Rosmarinus officinalis</i> oil	anti-biofilm formation	not found
	<i>Citrus aurantium bergamia</i> (bergamot) peel oil	fragrance agent	not found
	<i>Citrus grandis</i> (grapefruit) peel oil	antimicrobial activity: inhibits metabolism of and kill plaque bacteria	not found
	<i>Citrus aurantium dulcis</i> (orange) peel oil	fragrance agent	not found
	<i>Thymus vulgaris</i> oil	antimicrobial activity comparable to clorexidine or triclosan against <i>S. mutans</i> <sup>68</sup>	not found
	<i>Eugenia caryophyllus</i> (clove) leaf oil	antimicrobial agent	not found
	<i>Chamomilla recutita</i> flower extract	anti-inflammatory agent	not found
	<i>Pimpinella anisum</i> oil	antioxidant and antimicrobial agent <sup>69</sup>	not found
	<i>Foeniculum vulgare</i> fruit extract (fennel)	antibacterial agent active on <i>S. mutans</i> <sup>70</sup>	not found
	<i>Hamamelis virginiana</i> flower water	antioxidant and anti-inflammatory agent	not found
	<i>Malva sylvestris</i> (mallow) extract	active against <i>S. mutans</i> and <i>S. aureus</i> <sup>71</sup>	not found

Purpose and known adverse events of active toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse events
Vegetable-based ingredients	<i>Commiphora abyssinica</i> resin extract	antiseptic agent	not found
	<i>Commiphora myrrha</i> extract	antiseptic agent	not found
	<i>Malva officinalis</i> flower extract	active against <i>S. mutans</i> , <i>S. aureus</i> <sup>71</sup>	not found
	<i>Calendula officinalis</i> flower extract	active in preventing gingivitis, periodontal disease, stomatitis, and halitosis <sup>72</sup>	not found
	<i>Illicium verum</i> fruit/seed oil (star anise)	antibacterial and antifungal activity, especially active on <i>Staphylococcus aureus</i> <sup>73</sup>	not found
	<i>Rosa canina</i> fruit extract	antibacterial, antioxidant, astringent agent	not found
	<i>Avena sativa</i> extract	humectant agent	not found
	<i>Chondrus crispus</i> (carrageenan) extract	antimicrobial agent	not found
	<i>Aesculus hippocastanum</i> (horse chestnut) seed extract	matrix metalloproteinase inhibitor <sup>74</sup>	not found
	Carbon of beech and <i>Betulla</i>	whitening efficacy	not found
	<i>Aesculus hippocastanum</i> (horse chestnut) bark extract	matrix metalloproteinase inhibitor <sup>74</sup>	not found
	<i>Arum maculatum</i> root extract	antimicrobial activity against <i>S. aureus</i> <sup>75</sup>	not found
	<i>Melia azadirachta</i> leaf extract	anti-biofilm activity	not found
	peat moss extract	anti-biofilm activity	not found
	<i>Prunus spinosa</i> fruit juice	phenolic components and antioxidant activity <sup>76</sup>	not found
	<i>Simmondsia chinensis</i> (jojoba) seed oil	antimicrobial activity against <i>S. aureus</i>	not found
	<i>Juglans regia</i> (walnut) oil extract	anticariogenic <sup>77</sup> and anti- <i>Candida albicans</i> activity <sup>78</sup>	not found
	papain	anticariogenic, <sup>79</sup> anti-biofilm formation; effectively digests the main actinomyces fimbrial proteins, fimP and fimA <sup>80</sup>	not found
	bromelain	antimicrobial, <sup>81</sup> antiplaque and antigingivitis, <sup>82</sup> adjuvant in treatment of periodontitis <sup>83</sup>	not found
	<i>Petroselinum sativum</i> oil	antimicrobial agent active on <i>Streptococcus mutans</i> <sup>84</sup>	not found
	<i>Berberis vulgaris</i> extract	antimicrobial agent <sup>85</sup> ; inhibits collagenase activity of <i>Aggregatibacter actinomycetemcomitans</i> and <i>Porphyromonas gingivalis</i> <sup>86</sup>	not found
	<i>Eucalyptus globulus</i> oil	anti-inflammatory agent	not found
	<i>Cinnamomum zeylanicum</i> oil	active against <i>S. mutans</i> , <i>S. aureus</i> and <i>Candida albicans</i>	not found
	stevioside	natural sweetener <sup>87</sup>	not found
	<i>Glycyrrhiza glabra</i> (licorice) root extract	anti-inflammatory, antioxidant <sup>88</sup>	not found
	<i>Leptospermum scoparium</i> branch/leaf oil (Manuka oil)	strong antibacterial activity against periodontopathic and cariogenic bacteria ( <i>Porphyromonas gingivalis</i> , <i>Actinobacillus actinomycetemcomitans</i> , <i>Fusobacterium nucleatum</i> , <i>S. mutans</i> , and <i>S. sobrinus</i> ) <sup>89</sup>	not found
<i>Colocasia antiquorum</i> extract	antioxidant, effective in the treatment of aphthous ulcers <sup>90</sup>	not found	
Biological additives	maris sal (dead sea salt)	saliva flow stimulation	not found
	propolis cera	mucositis-effective <sup>91</sup>	not found
Antioxidants	<i>Ammonium glycyrrhizate</i> (licorice root)	anti-inflammatory, antioxidant <sup>88</sup>	not found
	xanthophyll	antioxidant	not found
Vitamins	<i>Styrax benzoin</i> extract	antioxidant <sup>92</sup>	not found
	cyanocobalamin (vitamin B12)	vitamin <sup>93</sup>	not found



## Identification of inactive ingredients

Seventeen of the 156 ingredients were classified as inactive. They were subdivided into sweeteners, flavorings, natural colorants, and fragrances. Of these, 9 (52.9%) were reportedly associated with a known AE, while 8 (47.1%) were not.

Among the inactive ingredients, 14 (82.4%) were natural ingredients, including organic essential oils ( $n = 8$ ), natural colorants ( $n = 3$ ; natural red, Carbo vegetabilis and natural green (chlorophyll) – CI 75810), natural flavoring agents ( $n = 2$ ), and one natural sweetener (*Stevia rebaudiana*).

The reported AEs were skin and eye irritations (coumarin, citronella, geraniol, linalool, cinnamaldehyde, and limonene) and gastrointestinal symptoms (sorbitol).

Table 2 presents the inactive ingredients with their purposes and known AEs. Adverse events are listed in the table, when appropriate.

Table 3 presents the classification of the ingredients and the percentage of AEs among the groups.

The research dataset is available from the corresponding author on reasonable request. All the ingredients are classified and listed in the table according to each of the examined formulations. Moreover, the International Nomenclature of Cosmetic Ingredients (INCI) for each of the examined formulations is reported.

## Discussion

This study identified for the first time the ingredients of 46 all-natural organic toothpastes currently marketed in Europe and classified them into active and inactive compounds. The study also evaluated, through a broad literature review, the purpose of the ingredients, as well as their known toxicity risks. In total, 156 unique ingredients were analyzed: 89.1% ( $n = 139$ ) and 10.9% ( $n = 17$ ) were classified as active and inactive, respectively.

According to our study, only 20.5% of the ingredients found in the organic toothpastes were associated with AEs, reassuring the safety of these products for oral care.

Table 2. Description of inactive ingredients with possible adverse events

Purpose and known adverse events of inactive toothpaste ingredients			
Type of ingredient	Ingredient	Purpose	Known adverse event
Sweeteners	sodium saccharin	artificial sweetener <sup>1</sup>	mixed findings; considered safe for consumption, <sup>1</sup> but new research states that it contributes to enamel demineralization <sup>2</sup>
	<i>Stevia rebaudiana</i> (leaf) extract	bio-sweetener, <sup>3</sup> antioxidant activity <sup>4</sup>	not reported
	sorbitol	substitute for sugar used as a sweetening agent <sup>1</sup>	reported to cause abdominal discomfort <sup>5</sup>
Flavorings	flavoring agent	functions as a flavoring agent <sup>6</sup>	has been shown to cause allergic reactions, such as inflammation of the mouth and lips and gingivitis <sup>6</sup>
	menthol	functions as a flavoring and scent for a toothpaste <sup>7</sup>	no known contamination risks <sup>7</sup>
	<i>Commiphora myrrha</i> resin extract	functions as a flavoring and scent for toothpaste and a natural anti-septic	no known contamination risks <sup>8</sup>
Natural colorants	CI 75810 (natural green (chlorophyll))	natural green pigment	no known contamination risks <sup>9</sup>
	CI 77268:1 (Carbo vegetabilis)	cosmetic colorant	not reported
	CI 75470 (natural red)	cosmetic colorant	not reported
Fragrances	limonene	flavor and fragrance additive, <sup>10</sup> derived from <i>Citrus aurantiifolia</i> oil	generally recognized as safe; case reports on irritant effect on eyes, nose, throat and skin; also, found to cause kidney damage in rats, but similar results were not found in humans <sup>7</sup>
	cinnamaldehyde	flavor and fragrance additive	strong evidence: human immune system toxicant or allergen; not suspected to be bio-accumulative <sup>11</sup>
	linalool	flavor and fragrance additive	skin, eye and respiratory tract irritant; not suspected to be bio-accumulative <sup>11</sup>
	eugenol	flavor and fragrance additive	classified as safe <sup>12</sup>
	citral	derived from <i>Citrus aurantiifolia</i> oil flavor and fragrance additive	no known contamination risks
	geraniol	flavor and fragrance additive	dangerous in case of ingestion and inhalation; marginally hazardous in case of skin contact (permeator), skin and eye irritant <sup>11</sup>
	citronella	flavor and fragrance additive	hazardous in case of ingestion; skin and eye irritant
	coumarin	flavor and fragrance additive	extremely hazardous in case of ingestion and inhalation; skin and eye irritant; severe overexposure can result in death; potential chronic carcinogenic effects (classified 2B, possible for humans according to the standard IARC classification) <sup>13</sup>



Table 3. Classification of ingredients

Ingredients	<i>n</i>	Safe <i>n</i> (%)	With AEs <i>n</i> (%)
fluorides	2	1 (50)	1 (50)
emulsifiers	19	12 (63.15)	7 (36.85)
emollients	4	4 (100)	0
buffering agents	4	1 (25)	3 (75)
preserving agents	6	0	6 (100)
thickening agents	3	0	3 (100)
abrasives	4	3 (75)	1 (25)
Active whitening/plaque removal agents	7	2 (28.6)	5 (72.4)
wetting agents	4	3 (75)	1 (25)
solvents	3	3 (100)	0
absorbents	4	4 (100)	0
antibacterials	5	5 (100)	0
active plant/herbal extracts	74	71 (96)	3 (4)
total	139	109 (78.4)	30 (21.6)
sweeteners	3	1 (33.3)	2 (66.7)
natural colorants	3	3 (100)	0
Inactive flavorings	3	2 (66.7)	1 (33.3)
fragrances	8	2 (25)	6 (75)
total	17	8 (47)	9 (53)

AEs – adverse events.

In detail, the study determined that most of the potential toxicity of the products was in the inactive ingredients.

The findings of this study are relevant to the following issues:

1. Compared with the results of the Basch and Kernan study on the composition of non-organic toothpastes for children, the percentage of ingredients associated with possible AEs in this study was much lower (75.6% compared to 20.5%). The Basch and Kernan study identified 71.1% and 28.9% of all components as active and inactive ingredients, respectively, while they were 89.1% and 10.9%, respectively, in this study.<sup>8</sup>

2. Most of the possible AEs associated with non-organic products do not occur with organic toothpastes. In particular, only 2 of the toothpaste formulations evaluated in this study contained the 2 classes of ingredients most frequently associated with toxicity, namely, synthetic polymers (e.g., polyethylene glycol (PEG), carbomers and Triclosan) and detergent agents (e.g., sodium lauryl sulfate (SLS)). This indicates favorable biocompatibility for the other 44 products. Synthetic polymers and detergent agents were present in only 2 formulations by one manufacturer (Cattier). The literature reports that non-ionic surfactants (e.g., PEG) act as penetration enhancers by decreasing surface tension and conditioning the stratum corneum, which may increase the diffusion of other molecules through the skin.<sup>10</sup> Moreover, there is evidence

on the side effects of detergent agents (e.g., SLS) that can cause irritation and soft tissue peeling.<sup>11–13</sup> Sodium lauryl sulfate is reported to be the most toxic agent on mucosal cells; it causes epithelial desquamation,<sup>14,15</sup> as shown by studies on the cytotoxicity and genotoxicity of commercial toothpastes.<sup>16–18</sup>

This study did not identify any artificial colorings, such as FD&C Blue No. 1 Lake, D&C Red No. 30 Lake, D&C Red No. 28, and Red No. 40, which are associated with allergic reactions, neurotoxicity, carcinogenicity, and skin discoloration.<sup>19–21</sup> In addition, there were no foam or flavor boosters, such as cocamidopropyl betaine, in the organic toothpaste formulations. Although rare, these compounds can cause allergic reactions.<sup>22,23</sup>

3. Most potential AEs associated with organic products are due to inactive ingredients, such as fragrances that can cause skin and eye irritations. In addition, the authors need to highlight that the study searched for any potential toxicity, regardless of the dose. This results in the conclusion that the very low absolute dose in these toothpastes is unlikely to cause such AEs. Furthermore, detailed information on the concentration (%) of each ingredient is missing, which is challenging for researchers.

Twenty-seven (58.7%) formulations contained a sweetening agent, including 25 (92.6%) with sorbitol, one (3.7%) with sodium saccharine, and one (3.7%) with *Stevia rebaudiana*. *Stevia rebaudiana* is a sweetening agent that has no reported AEs, so it meets the safety standards of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Recent research suggests that sodium saccharine, although safe for consumption,<sup>24</sup> contributes to enamel demineralization.<sup>25</sup> Sorbitol has been shown to cause abdominal discomfort and diarrhea.<sup>26</sup> Conversely, a recent review by de Cock et al.<sup>27</sup> highlights the extensive research on the safety of erythritol, a polyol produced by the natural process of fermentation. Erythritol has sweetness and caloric reduction compared to sucrose, no cariogenic potential, a low glycemic index, a relatively high stability in acidic and alkaline environments, a high stability against heat, and suitability as a bulking agent in food manufacturing. Furthermore, there is a significant number of toxicology and safety studies that report a lack of AEs associated with small amounts of erythritol.<sup>9,28,29</sup> Analogous characteristics of safety and health effects are valid for xylitol. Considering this evidence, the authors propose the use of *Stevia rebaudiana*, erythritol or xylitol in toothpaste formulations instead of other components that have been linked to AEs.

Regarding fragrances, the authors suggest focusing on 100% naturally sourced, plant-based essential oils to avoid possible AEs. Moreover, they recommend that as small a quantity as possible should be used to avoid potential AEs.

Essential oils should have 3 major characteristics: safe to consume, pure food grade, and organic certification. Alternatively, naturally derived flowers, spices and fruit flavors are suitable options, especially for children's toothpaste.

In the past, the risk of bioaccumulation had been correlated with the amount of toothpaste inadvertently swallowed during brushing.<sup>30</sup> Consequently, the American Dental Association (ADA) recommendations stated that no amount of toothpaste should ever be swallowed intentionally.<sup>31</sup> Therefore, based on the results of a recent randomized placebo-controlled study that evaluated the effect of a vitamin B12-fortified toothpaste on vitamin status markers in vegans, manufacturers should be cautious when selecting toothpaste ingredients. This is because each toothpaste ingredient, when in contact with the oral cavity, can also enter the systemic blood circulation via the sublingual blood system route. The study demonstrated that, compared to the placebo, the vitamin B12-fortified toothpaste resulted in a significant increase in serum vitamin B12 concentration after 12 weeks. Although the authors specified that the mechanism of vitamin B12 absorption via the mucosal barrier is currently not known, the toothpaste-based strategy may be a promising approach for delivering vitamins.<sup>32</sup>

While there are few existing trials evaluating the clinical effectiveness of organic toothpastes, there appears to be a rising trend. It is necessary to obtain scientific evidence of abrasive action, removal of external discoloration, and remineralizing effects on enamel. Interestingly, only 8 (17.4%) of the toothpastes analyzed in this study were fluoridated: 6 (13%) with sodium fluoride and 2 (4.3%) with monofluorophosphate. The remineralizing effect of fluoride on International Caries Detection and Assessment System (ICDAS)-II codes 1 and 2 early carious lesions is well understood.<sup>33</sup> Considering this data, many questions and doubts arise about the remineralizing effects of organic toothpastes; answering them as soon as possible is fundamental to promote their use and provide both clinicians and patients with clinical recommendations based on evidence.

A recent systematic review highlighted the efficacy of *Camellia sinensis* extracts on gingivitis and periodontitis.<sup>34</sup> Thus, it is surprising that it was present in only 2 of the 46 toothpaste formulations analyzed in this study. A recent clinical study found that scaling and root planing with the aid of ozonated olive oil mouthwash were more effective on salivary matrix metalloproteinase-8 (MMP-8) reduction than scaling and root planing alone.<sup>35</sup> None of the examined formulations contained ozonated olive oil. The supplementary research database is available from the corresponding author on reasonable request. All of the listed single ingredients can be searched.

In the light of the above, the authors of this article emphasize the need for direct comparisons between manufacturers and researchers. It is only through constant dialogue and inclusive cooperation between the manufacturers and those conducting the research that products requested by patients can be obtained. In fact, patients are increasingly oriented toward ecologi-

cal transition and sustainability, given the development of dentistry itself toward less invasive procedures that also consider the patient's quality of life.<sup>36–38</sup>

## Limitations

The main limitation of this study is that it only included one supermarket chain in one country. However, the authors showed that most products are marketed in more than 6 European countries, which diminishes the impact of this limitation. Another limitation is that the toxicity evaluation was based on evidence emerging from our literature search, which did not assess the actual quantity (see above) or possible combinations; these could be considered worst-case scenarios. Third, the authors did not conduct a direct comparison between organic and non-organic toothpaste formulations. However, the difference between the analysis in this study and previous analyses is sufficient to minimize this bias. Finally, the efficacy was not assessed. Future research is warranted to further evaluate organic toothpastes and address these limitations.

## Conclusions

Based on the results of this study, the organic toothpaste formulations showed adequate safety when each ingredient was analyzed. However, the clinical efficacy of the organic toothpastes still needs to be assessed to support their daily use for maintaining oral health and preventing diseases. This analysis provides important information for consumers who are concerned with ecological and environmental issues.

## Ethics approval and consent to participate

Not applicable.

## Data availability


The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.


## Consent for publication


Not applicable.


## ORCID iDs


Marta Mazur  <https://orcid.org/0000-0002-0525-681X>

Artнора Ndokaj  <https://orcid.org/0000-0002-1400-8607>

Sabina Bietolini  <https://orcid.org/0000-0002-4736-8182>

Veronica Nisii  <https://orcid.org/0000-0003-3801-1357>

Irena Duš-Ilnicka  <https://orcid.org/0000-0002-4745-2560>

Livia Ottolenghi  <https://orcid.org/0000-0001-7390-4316>

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