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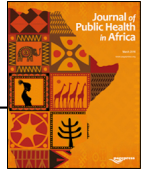
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REVIEW

Chemical vs. natural toothpaste: which formulas for which properties? A scoping review

Aïda Kanouté^{1*} | Serigne Ndamé Dieng¹ | Mbathio Diop¹ | Amadou Dieng¹
| Ayotollah Khoumeïni Sene² | Massamba Diouf¹ | Cheikh Mbacké Lo¹ | Daouda Faye¹
| Florence Carrouel³

¹Public Health Service, Institute of Dentistry and Stomatology, Faculty of Medicine, Pharmacy and Dentistry, Cheikh Anta Diop University of Dakar, Senegal

²Oral service District of Kaffrine Ministry of Health and Social Action, Dakar, Senegal

³Faculty of Medicine, Dr. Aïda Kanouté Public Health Service Institute of Dentistry and Stomatology, Faculty of Medicine, Pharmacy and Dentistry Cheikh Anta Diop, Laboratory Systemic Health Pathway, UR University of Lyon 1, France

Abstract

Introduction. The proliferation of the oral care industry has made it more challenging for shoppers to zero in on the best possible toothpaste for their preventative requirements. It also makes the toothpaste's various components safer.

Objective. The researchers set out to evaluate the state of information about the biological properties and cytotoxicity of adult toothpaste so that they might make some informed recommendations.

Methods. A scoping review of research published between 2015 and 2020 according to PRISMA guidelines was performed.

Results. *In vitro* clinical trials account for 44% of the papers, *in vivo* clinical trials for 25%, systematic reviews for 19%, and meta-analyses for 12%. They have active chemical components that have been shown to be antimicrobial, anti-inflammatory, or desensitizing. Herbal toothpaste has these characteristics and is very secure to use. Toothpaste with sodium lauryl sulfate has been found to be harmful.

Conclusions. Scientists have investigated the biological effects of a wide range of chemically active compounds and plant extracts. Herbal toothpaste, it has been discovered, is both efficient and secure. Companies making toothpaste should be required to clearly label the product's qualities, active ingredients, and potentially harmful ingredients on the packaging.

Keywords: Adults, Properties, Toothpaste, Formulas.

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INTRODUCTION

Oral diseases like caries and periodontitis affect people all over the world and cause a lot of stress and cost for both individuals and health systems.^{1,2} Literature says that 46.2% of people around the world have caries in their primary teeth,³ 47% have untreated decayed teeth, and 9.8% have severe periodontitis.⁴ The best way to fight these oral diseases and all of their effects seems to be to keep them from happening in the first place.⁵ Dental plaque control is the most important thing you can do to keep your teeth healthy.⁶ Mechanical control of microbial plaque is necessary to prevent dysbiosis of the oral microbiota and the development of oral disease. Chemical control, on the other hand, seems to be a complementary treatment that helps with elimination and stops microbial dysbiosis. This could make people less dependent on mechanical oral care.⁶ Toothpaste seems to be the most important chemical product used to keep teeth clean.^{4,6} Toothpaste has both active and inactive ingredients.⁷⁻⁹ Its biological properties come from the things that make it work (antibacterial, anti-inflammatory or desensitizing).^{10,11} Toothpaste is stable, flows well, and tastes good because of the ingredients.⁹ For a very long time, toothpaste with chemical agents has been the most popular way to keep your teeth clean. In the last few decades, however, there has been a rise in natural toothpaste, which has been shown to have anti-inflammatory and antimicrobial properties.¹²⁻¹⁴ "Natural" toothpaste usually doesn't have things like preservatives, artificial sweeteners, artificial colors, additives, or synthetic flavors and fragrances.¹⁵ These kinds of "natural" toothpaste have coconut oil, clove oil, *Carica papaya* leaf extract, *Matricaria recutita*, *Azadirachta indica*, *Aloe vera*, and *Calendula officinalis* in them. Most of the ingredients in these "natural" toothpastes are extracts from plants that have been used as medicine for thousands of years all over the world.⁹

In pharmacies and supermarkets, numerous toothpaste formulations from various manufacturers are available. Each has unique qualities, and the composition varies according to the disease or condition to be prevented or treated. Such a varied

makeup has generated questions about the cytotoxicity of specific components.¹ Sodium lauryl sulfate (SLS), propylparaben, triclosan, and allergens such as methylchloroisothiazolinone and methylisothiazolinone are allergens found in some toothpastes that pose a threat to human health.²³⁻²⁶ Some of these drugs have negative side effects, such as altered taste and discolored teeth, and their deleterious effects on endocrine function, including fertility, are uncertain.²⁷⁻²⁹ Fluoride, which is beneficial for preventing caries lesions, might have negative side effects.³⁰ Absorption of excessive fluoride through the gastrointestinal system can be hazardous to bone at very high doses (bone fluorosis) and developing teeth at modest doses (dental fluorosis).³¹ Some producers have moved away from SLS, chlorhexidine, and triclosan and have introduced new, less irritating surfactants, such as nonionic polyethylene glycol ethers of stearic acid.^{32,33} Since the market for oral hygiene products, particularly toothpastes, is expanding rapidly, it is crucial to understand their chemical makeup and the good or negative impacts of the chemicals. Thus, the community would be able to make decisions based on their needs, and dentists would be able to administer medications based on their patients' dental health issues. The following research questions come to mind: What components are responsible for the biological features of toothpastes? What ingredients are responsible for toothpastes' cytotoxic properties? The purpose of this review was to give some recommendations based on what we know about toothpaste properties.

Supplementary information The online version of this article ([Figures/Tables](#)) contains supplementary material, which is available to authorized users.

Corresponding Author: *Aïda Kanouté, Public Health Service, Institute of Dentistry and Stomatology, Faculty of Medicine, Pharmacy and Dentistry, Cheikh Anta Diop University of Dakar, Fann, BP: 5005 Dakar, Senegal. Tél: +221.776552322*
Email: aida.kanoute@gmail.com

MATERIALS AND METHODS

Type of study

A scoping review was carried out according to the Preferred Report Items for Systematic Reviews and Meta-Analyses for scoping review (PRISMA-ScR) matrix guidelines (Supplementary Sc. material 1).³⁴

Publication research strategy

The literature search was primarily done on Medline, Science Direct, and Google Scholar. The references of the studies found were also searched for relevancy. Keywords such as “toothpaste”; “chemical toothpaste”; “property”; “composition”; “herbal”; “adult”; “toxicity” were used to query the data sources. Two independent investigators carried out the article research and selection.

Selection and eligibility of publications

En eligible study should be a randomized clinical trial (CT), a non-randomized clinical trial, a systematic review, or a meta-analysis that includes CTs; about biological properties or the cytotoxicity of adult toothpaste, published between 2015 and 2020 and accessible. This procedure minimized selection bias. For selection, a sequenced strategy was chosen. First, duplicated articles were eliminated, then studies that were consistent with the eligibility criteria were selected based on their titles and abstracts and finally, eligible studies were selected based on their full content.

Quality of selected studies

The study's quality was assessed using the Critical Appraisal Tools by the Joanna Briggs Institute (JBI) of the Faculty of Health Sciences at the University of Adelaide in Australia. These are questionnaires for analytical assessments of study.³⁵ Based on the percentages of favorable responses to the items, the studies were classified as low, moderate, and high quality. A study with less than 50% of favorable responses was considered to be of “low quality”; between 50 and 70%, of favorable responses the study was considered to be of “moderate quality”; at more than 70% of favorable responses, the quality of the study was considered to be “high”. Thus, 56% of the studies were of “high” quality and 44% of “moderate” quality.

Study variables

The variables studied are of the qualitative type. These are antibacterial, anti-inflammatory, desensitizing and anti-halitosis properties of toothpaste, as well as cytotoxicity and composition. Antibacterial properties include action against plaque and tooth decay. The anti-inflammatory properties are linked in particular to the action against gingivitis, while the desensitizing action corresponds to the therapeutic properties against dental hypersensitivity. Cytotoxicity relates to the undesirable effects caused by the components of toothpaste. All these variables are dichotomous (yes/no). The composition of the toothpaste relates specifically to the active principles and certain excipients.”

Data collection

The review was carried out from July 2020 to October 2020, and the same independent investigators performed the data retrieval. For this work, two grids were made; the first contains the article's description and the second the summary of obtained data according to the predefined variables.

Analysis framework

A comprehensive narrative of the results was made. With percentages and numbers, the study's characteristics were described by their study variables. The toothpaste composition was described with emphasis on active agents associated with each biological property or cytotoxicity.

RESULTS

Selection and description of studies

The literature search had yielded 2,329 articles. After deleting duplicates, 1,405 articles remained, of which 1,362 were eliminated based on their titles and abstracts. Of the remaining 43, 16 articles were retained for analysis after a second selection from reading the full text. Thus, 27 studies were eliminated for these reasons: six (6) studies related to children and adolescents; four (4) were inaccessible items; fourteen (14) do not specifically mention toothpaste and three (3) whose toothpaste composition was unknown (Figure 1).

CHEMICAL VS. NATURAL TOOTHPASTE

The 16 eligible studies for analysis comprised three (19%) systematic reviews, two (12%) meta-analyses, seven (44%) in-vitro clinical trials and four (25%) *in vivo* clinical trials. Nine of them (56%) were about chemical toothpaste, five (31%) about herbal toothpaste, and two (13%) about mixt toothpaste. Six of them (40%) have been carried out on the antibacterial effects, four (27%) on inflammatory properties, four (27%) on desensitizing actions and one on (6%) halitosis. Only four papers or 24% were about the toxicity of toothpaste components (Table 1).

TOOTHPASTE PROPERTIES AND COMPOSITION

Antibacterial active agents

The results have shown that the sodium fluoride and stannous ions, arginine, triclosan and sodium bicarbonate produce the chemical toothpaste's antibacterial properties. While the herbal toothpaste active agents are extracts of aloe-vera leaves, demelaleuca alternifolia, calendula, Origanum essential oils (dubium *Boiss* and *Cinnamomum cassia*), clove, and thyn (especially on *Streptococcus mutans* and *aureus*) and polyherbal (comprising artemisia, *Satureja khuzestanica* and *Myrtus communis*) (Supplementary 2).

Anti-inflammatory active agents

The results suggest that chemical toothpaste with stannous fluoride, chlorhexidine and sodium bicarbonate have substantial anti-inflammatory effects. Two clinical trials concluded that there was a significant improvement in periodontal indices after usage of toothpaste containing extracts of *Chamomilla recutita*, *Salvia officinalis*, arnica montana, *Echinacea purpurea*, *Rhizoma chuanxiong* and *Rhizoma imperatae* (for a treatment of 8 weeks or more). The aloe vera was not significantly effective against gingivitis (Supplementary 3).

Desensitizing active agents

According to the results on chemical toothpaste, the main active agents effective against dental hypersensitivity are nano-fluorinated bioactive glasses and zinc nano-oxide at low concentration, arginine 8%, sodium calcium phosphosilicate, nano hydroxyapatite, potassium nitrate. The arginine and the

nano hydroxyapatite have a longer duration of action while the potassium nitrate has a short and rapid one. As for herbal toothpaste, extracts of Indian plants such as suryakshara, palakya, lavanga and triphala had a desensitizing in vitro efficiency (Supplementary 4).

Active agents against halitosis

Results of a systematic review have suggested that stannous fluorides, when used repeatedly with mechanical action, can significantly reduce halitosis.

Toothpaste cytotoxicity

The results have shown *in vitro* cytotoxicity of toothpaste containing sodium lauryl sulfate and cocamidodropyl betaine.

No studies have noted the cytotoxicity of herbal toothpaste (Supplementary 5).

DISCUSSION

This scoping review included six studies on the antibacterial effects of toothpaste. As chemical antibacterial active agents, they have mostly identified fluorides (sodium or stannous), triclosan, and arginine; for natural toothpaste, the active ingredients are primarily extracts of aloe vera leaf, demelaleuca alternifolia, calendula, essential oils, and polyherbal. Plaque is greatly diminished by sodium fluoride concentrations of 1,450 ppm or greater. This research confirms the literature highlighting the bactericidal and bacteriostatic capabilities of sodium fluorides by demonstrating that they hinder the development and metabolism of bacteria.⁵² The results indicate a reduction in dental plaque ranging from 1.6% to 25.8% between 24 hours and six months of stannous fluoride toothpaste use. A randomized clinical research revealed that stannous fluorides limit the growth of multi-species biofilm.⁵³ Fluorides can influence bacterial metabolism in a variety of ways that involve fundamentally distinct mechanisms.⁵⁴ They can function as enzyme inhibitors directly. In addition, they can result in the development of metal-fluoride complexes that block proton-translocating F-ATPases. However, their behavior would be primarily influenced by their weak acidic personality. Fluorides enhance membrane proton permeabil-

ity and impair the activity of F-ATPases in proton export, generating cytoplasmic acidification and glycolytic enzyme inhibition. Thus, fluorides reduce bacteria's acid resistance. They perform best at acidic pH levels. Under the acidic circumstances of cariogenic plaque, fluorides at concentrations as low as 0.1 mM can fully halt *Streptococcus mutans* glycolysis.⁵⁴

Toothpaste formulations combining triclosan and arginine were highly efficient against *Streptococcus mutans* and *Candida albicans*. According to Riley et al., triclosan can reduce tooth plaque by 22% and dental caries by 5%.⁵⁵ Depending on its concentration, triclosan can be bacteriostatic or bactericidal.⁵⁶ Triclosan can function as an antibacterial agent by interfering with the stability and topology of lipid and protein structures, or by compromising the membrane's integrity. Triclosan can also damage the structure of proteins, so inhibiting their biological function. Triclosan affects the fatty acid synthesis⁵⁷ in bacteria. The research of Huang et al. indicates that brushing with toothpaste containing arginine decreases dental biofilm⁵⁸ biomass. This antibacterial effect of arginine may be owing to arginine's ability to promote membrane permeability.⁵⁹

In addition to chemically active ingredients, toothpaste containing plant extracts possesses antibacterial characteristics. Growth of oral bacteria is inhibited by aloe vera.⁶⁰ Although there are insufficient investigations on *Calendula officinalis* toothpaste, in-vitro antibacterial activity has been observed in mouthwashes.^{61,62} Specifically against *S. mutans* and *L. lactis*, toothpaste containing essential oils of cinnamon, clove, oregano, and thyme has demonstrated considerable antibacterial activity. These essential oils are mostly composed of carvacrol, eucalyptol, linalyl acetate, and eugenol, which affect the permeability of cells and harm the bacterial cell wall. According to a test conducted in Iran, toothpaste containing artemisia leaf extract, *Satureja khuzestanica*, and *Myrtus communis* inhibits bacterial growth *in vitro*. These results are similar with the findings of Sekar et al., who found that most bacterial species are sensitive to multiherbal toothpaste.⁶³ Their antibacterial effectiveness is believed to be mostly attributable to alkaloid, flavonoid, polyphenols, and lecstannous.⁶⁴

Review demonstrates anti-inflammatory properties of toothpaste containing stannous fluoride, sodium bicarbonate, and chlorhexidine, as well as natural toothpaste containing chamomilla recutita, salvia officinalis, arnica montana, echinacea purpurea, rhizoma chuanxiong, and rhizoma imperatae extracts. Those containing stannous fluoride diminish gingival irritation considerably. According to the findings of a study by Paraskevas et al., stannous fluoride can reduce periodontopathogenic plaque and gingivitis.⁶⁵ As a result of adsorption on the filmy enamel surface,³⁶ chlorhexidine exerts an immediate bactericidal effect and a protracted bacteriostatic effect. A thorough evaluation suggests that brushing with toothpaste containing chlorhexidine decreases plaque and gingivitis significantly.⁶⁶ According to Hosadurga et al., Parodontax toothpaste with chamomile extracts significantly lowers gingival inflammation.⁶⁷ *Rhizoma chuanxiong* and *Rhizoma imperatae* are primarily anti-inflammatory and reduce gingival bleeding considerably.⁴⁸ The *Rhizoma chuanxiong* constituent senkyunolide inhibits the NF-kappa B pathway or the synthesis of pro-inflammatory mediators.⁶⁸

This review also suggests that toothpaste containing nano-fluoride and nano zinc oxide bioactive glasses, arginine, sodium calcium phosphosilicate, nano hydroxyapatite, potassium nitrate, and stannous fluoride is useful against dental hypersensitivity. To treat dental hypersensitivity (DH), the dentinal tubules must be occluded and the nerve transmission, which creates the nociceptive sensation, must be interrupted. Bekes et al. demonstrated that nano-fluoride glasses and zinc fluorides have a greater potential for bioactive tubular occlusion than ordinary fluorides.⁶⁹ Nano hydroxyapatites have the same composition and structure as the apatite crystal of dental enamel. Together with arginine, they create a stronger dental tubule plug, resulting in a longer duration of dental pain alleviation compared to potassium nitrate or fluoride.³⁹ The mechanism of potassium salts' desensitizing effect is nerve depolarization. This causes a disruption in the transmission of nociceptive information and, consequently, a reduction in tooth sensitivity.⁴³ The study demonstrates that toothpaste containing extracts of Indian plants, including suryakshara, palakya, lavanga, and

triphalā, is effective against dental hypersensitivity. However, very little research has been conducted on the desensitizing effects of herbal toothpaste. It is believed that the accumulation of granules resistant to solubilization causes tubular blockage.⁷⁰

Only one of the reviewed studies examined the effectiveness of toothpaste against bad breath, and stannous fluoride toothpaste proved to be the most effective. The study by Feng et al. found that stannous fluoride toothpaste reduced bad breath more effectively than sodium fluorides.⁷¹ However, the underlying mechanism is not fully understood, but the indirect benefit via its anti-plaque qualities has been verified.

Some chemical toothpastes were found to be cytotoxic, but none of the herbal toothpastes were. Experiments on the cytotoxicity of some antibacterial, anti-inflammatory, and desensitizing toothpaste yielded substantial results.^{43,72} For all experimentally active drugs, however, preventive and non-toxic doses were utilized. Therefore, the reported toxicity was due to typical toothpaste detergents, sodium lauryl sulfate or cocamidodropyl betaine.⁷³ The clinical experiment conducted by Cvilk et al. confirmed that these two detergents are harmful to oral tissues. Unknown is the lethal threshold concentration of sodium lauryl sulfate in toothpaste, although its toxicity would also depend on its exposure.⁷⁴

These findings have implications for the field of public health. They justify actions of sensitization on the toxicity of some excipients, specifically sodium lauryl sulfate, which should not be maintained in the mouth for an extended period of time. The findings further support the need for regulation governing the labels on toothpaste tubes. Therefore, it would be required to explicitly disclose the names of the active chemicals, the quantity of these compounds, and

whether or not they pose a potential toxicity concern. Given the scientific proof of "natural" toothpaste's efficacy in oral prophylaxis, they demonstrate that there should be a growing interest in it.

The evaluation contains both strengths and weaknesses. Its adherence to the methodological criteria for conducting a review, in particular the participation of two independent investigators for article selection and data retrieval, is one of its strengths. However, several databases (Elsevier through Scopus) were inaccessible; considering the huge number of the databases investigated, the chance of selection bias is minimal.

CONCLUSIONS

By isolating the responsible active ingredients, the results of this systematic research have validated the known properties of some toothpastes. A knowledge update is required for diverse toothpaste formulations. It emphasizes the antibacterial, anti-inflammatory, and desensitizing properties of herbal toothpaste, as well as its safety. It provides genuine insights, particularly for topics requiring explanation. The concentrations or toxicity thresholds of components implicated in the harmful effects of toothpaste should be determined.

INFORMATION

Conflict of interest. The authors declare no potential conflict of interests related to this work.

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TABLE 1: Description of selected studies.

Authors and year of publication	Type of study	Type of tooth-pastes	Biological properties	Cytotoxicity
Valkenburg <i>et al.</i> 2019 (36)	Systematic re-view	Chemical	Anti-inflammatory	No
Valkenburg <i>et al.</i> 2019 (37)	Systematic re-view	Mixed	Anti-inflammatory, Anti-bacterial	No
Johannsen <i>et al.</i> 2020 (38)	Systematic re-view	Chemical	Anti-inflammatory, Agains alitosis	No
Hu <i>et al.</i> 2019 (39)	Meta-analysis	Chemical	Desensitizing	No
Cunha-Cruz and Zeola 2019 (40)	Meta-analysis	Chemical	Desensitizing	No
Oliveira Carvalho <i>et al.</i> 2020 (41)	In vitro clinical trial	Herbal	Antibacterial	No
Vannet <i>et al.</i> 2015 (42)	In vitro clinical trial	Chemical	Yes
Anthony <i>et al.</i> 2020 (43)	In vitro clinical trial	Chemical	Desensitizing	No
Camargo <i>et al.</i> 2017 (44)	In vitro clinical trial	Chemical	Antibacterial	Yes
Sadeghi-Nejad <i>et al.</i> 2018 (45)	In vitro clinical trial	Herbal	Antibacterial	No
Karadağlıoğlu <i>et al.</i> 2019 (46)	In vitro clinical trial	Herbal	Antibacterial	No
Cviki <i>et al.</i> 2015 (47)	In vitro clinical trial	Chemical	Yes
Kar <i>et al.</i> 2019 (48)	In vitro clinical trial	Mixed	Desensitizing	No
He <i>et al.</i> 2019 (49)	In vitro clinical trial	Herbal	Anti-inflammatory	No
Orisakwe OE <i>et al.</i> 2016 (50)	In vitro clinical trial	Chemical	Yes
Kharaeva <i>et al.</i> 2020 (51)	In vitro clinical trial	Herbal	Anti-inflammatory	No

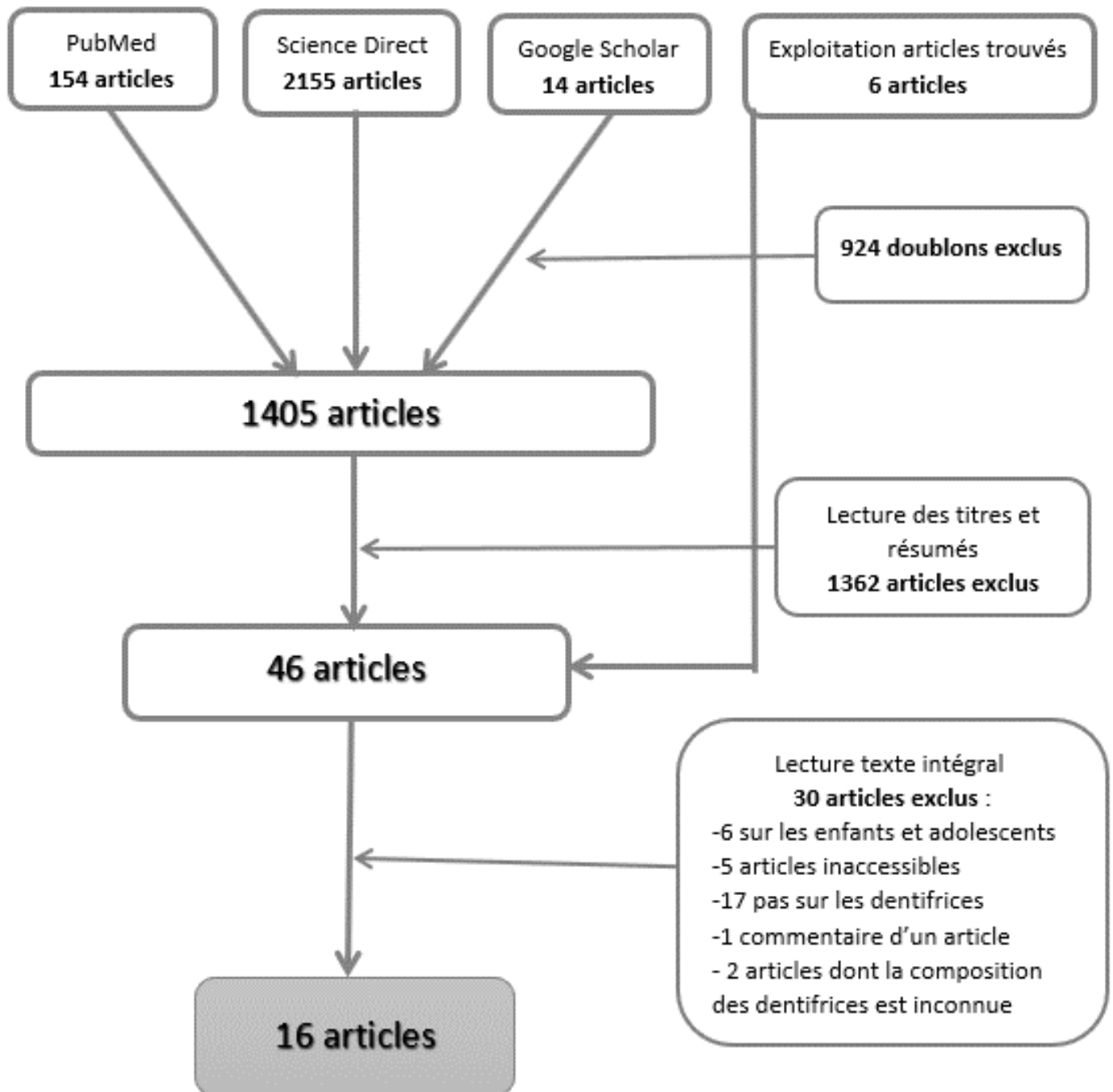


FIGURE 1: Flow-chart.

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