**Review Article**

*Camellia sinensis* in Dentistry: Technological Prospection and Scientific Evidence

Lídia Audrey Rocha Valadas, Rosueti Diógenes de Oliveira Filho, Edilson Martins Rodrigues Neto, Mary Anne Medeiros Bandeira, Marta Maria de França Fonteles, Vanara Florêncio Passos, Ana Cristina de Mello Fiallos, Marta Assef Leitao Lotif, Nara Juliana Custodio de Sena, Thereza Cristina Farias Botelho Dantas, Igor Lima Soares, Patricia Leal Dantas Lobo, and Aldo Fabian Squassi

1. Department of Preventive and Community Dentistry, University of Buenos Aires, Buenos Aires, Argentina
2. Pharmacy, Dentistry and Nursing College, Federal University of Ceará, Fortaleza, Brazil
3. Nova Esperança Nursing College (FACENE), Mossoró, Brazil
4. Paulo Picanço College of Dentistry, Fortaleza, Brazil
5. Unichristus, Fortaleza, Brazil

Correspondence should be addressed to Lídia Audrey Rocha Valadas; lidiavaladas@gmail.com

Received 18 March 2021; Revised 17 August 2021; Accepted 18 August 2021; Published 31 August 2021

**Academic Editor:** Amin Tamadon

Copyright © 2021 Lídia Audrey Rocha Valadas et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Purpose.** This study aimed to evaluate reports of patents for oral care formulations, based on *Camellia sinensis* (*C. sinensis*), deposited and granted in intellectual property banks. **Methods.** A survey was conducted through collection, treatment, and analysis of extracted information from patent reports selected. The documentary research was conducted in January 2021 on formulations with *C. sinensis* for dental applications, including since the first patent deposits until the current time. The risk of bias of clinical trials with these formulations was analyzed to verify the scientific evidence. The data extracted represent the distribution of the number of patents by banks, annual evolution of patent deposits, applicant of patents by country, distribution of patents according to International Patent Classification codes, and the types of patented products. **Results.** Data and information from 20 selected patents were extracted. The United States Patent and Trademark Office (USPTO) and World Intellectual Property Organization (WIPO) were the banks with the largest number of patents for formulations with *C. sinensis* for oral care applications with 7 (35%) and 6 (30%) patent registrations, respectively. Other banks did not provide patents related to the search. Patents of compositions were the largest with 14 filings, and the remainder of formulations are represented specially by mouthwashes and toothpastes. As for clinical application, 18 patents were filed as products with antimicrobial and antibiofilm action, while 2 patents are directed to the treatment of xerostomia. In general, the aspects of the studies of clinical efficacy pointed to a low risk of bias. **Conclusion.** The study pointed out a small number of products protected by patents for *Camellia sinensis* for oral care indication, highlighting mainly mouthwash compositions and formulations. In the methodological parameters of clinical trials carried out with the formulations, the majority pointed out a low risk of bias.

1. **Introduction**

The practice of using medicinal plants with pharmacological activities for the treatment of diseases is ancient, including for conditions related to oral health. The use of natural products as medicinal therapy existed long before the pharmaceutical industry and after the emergence of these products has been incorporated into the development of formulations to the present day [1–3].

Herbs and medicinal plants can be used in different ways, including whole herb, leaves, roots, essential oils, and prepared as teas, syrups, creams, ointments, and even
capsules or pills that contain a powdered form of the plant [4]. Tea constitutes an infusion prepared from dry leaves and is the second most consumed drink in the world, its consumption being surpassed only by water, in addition to having great cultural and economic relevance in several countries. Among the most varied types of teas, Camellia sinensis (C. sinensis) teas stand out as one of the most popular and used worldwide [5–7].

C. sinensis is a plant rich in polysaccharides, caffeine, polyphenols, amino acids, and antioxidants, in addition to micro and macronutrients beneficial to human health [8]. It has different important pharmacological properties such as antimicrobial, antioxidant, antidiabetic, and anti-inflammatory activities, in addition to its consumption presenting several documented benefits related to oral health, especially regarding caries and periodontal diseases [3, 6].

This plant is a species belonging to the Theaceae family and has small perennial shrubs, widely used to produce teas, especially green and black [9]. These teas have several pharmacological properties, with their production being carried out mainly in regions of tropical and subtropical climate, with abundant and regular rainfall [9, 10]. According to its fermentation and maturation process, C. sinensis tea can be classified as green, white, yellow, red, and black, where important differences can be verified according to its cultivation and leaf processing [6, 11].

Green tea from C. sinensis has a strong antioxidant power through its polyphenolic chemical constituents, beneficial in several clinical conditions such as dental caries, gingivitis, periodontitis, and halitosis, in addition to neuroprotection in the oral cavity [1]. Since it has a high concentration of fluoride in its nutrient composition, the consumption of this tea is extremely beneficial in repairing dental tissue in an acidic environment and improving resistance to demineralization [12, 13]. Furthermore, it has been shown that this tea has other properties, such as antiviral action against influenza viruses, herpes viruses, and antifungal action against Candida albicans, Trichophyton mentagrophytes, and Trichophyton rubrum [14].

Black tea is a product of C. sinensis treated with an oxidation process that requires longer steps and contains a greater amount of caffeine when compared to other teas from this plant. Its continued use can reduce blood pressure, the risks of type 2 diabetes, and improve the lipid profile. Its polyphenolic constituents promote health benefits, mainly in obesity, diabetes, cancer, atherosclerosis, inflammatory diseases, and osteoporosis [15–18].

In recent years, the search for new substances and formulations with pharmacological potential and biocompatibility has increased, which is revealed by the growing number of studies on the use of natural products. Often these studies seek to generate new technologies for society with a natural raw material traditionally used, giving rise to the development of innovations and patents [19, 20].

The elaboration of an invention patent or utility model is an extremely relevant indicator to mainly evaluate the level of development and technological innovation in industries and research institutions. Therefore, natural products are sources of biomolecules or therapeutic complexes that can be used for technological innovation and maintain competition in the market in several areas, including products for dental applications [21, 22]. Given the economic importance and medicinal products of C. sinensis, as well as its several benefits to systemic and mainly oral health, this study aimed to evaluate reports of patents deposited and granted on dental formulations based on C. sinensis in intellectual property banks.

2. Materials and Methods

2.1. Elaboration of the Technological Prospective Study. The survey was conducted through collection and analysis of extracted information from patent reports selected. The documentary research was conducted in January 2021 about formulations with C. sinensis for dental applications, including since the first patent deposit in 2004 until all the year of 2020. The searches were direct with access to reports of patents deposited and granted in the following intellectual property banks of worldwide references:

(1) Canadian Intellectual Property Office (CIPO)—Canada
(2) China National Intellectual Property Administration (CNIPA)—China
(3) Espacenet—European Patent Office (EPO)—Europe
(4) German Patent and Trademark Office (DPMA)—Germany
(5) Intellectual Property India—India
(6) Japanese Patent Office (JPO)—Japan
(7) National Institute of Intellectual Property (INPI)—Brazil
(8) Swiss Federal Institute of Patent Office (IGE-IPI)—Switzerland
(9) United States Patent and Trademark Office (USPTO)—United States
(10) World Intellectual Property Organization (WIPO)—Europe

2.2. Search Strategy and Data Extraction. For the preparation of the study, we conducted a mapping of patent applications using the keyword “Camellia sinensis” in the search field. All patent documents that included this term were initially considered in the search with the exploratory reading of titles and summaries, as a criterion for inclusion of the patents found. Then, only the active reports related to dentistry were selected; expired, abandoned, or denied patents were not included. Relevant information that describes the invention in the patent reports was selected and organized in graphics in GraphPad Prism 6 program to analyze descriptive statistics.

The data extracted represent the distribution of the number of patents by banks, annual evolution of patent
deposits, applicant of patents by country, distribution of patents according to International Patent Classification (IPC) codes, and the types of patented products.

2.3. Scientific Evidence. According to the patents selected at the end of the search, the described inventions and their purposes with dental applications were evaluated and were searched clinical trials related to each selected patent in PubMed.

2.4. Risk of Bias Assessment. Trials were assessed using Cochrane’s tool for assessing the risk of bias in randomized trials [23]. The tool includes the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. We rated each domain as low risk, unclear risk, or high risk of bias.

We classified the overall risk of bias as low if all domains were at low risk of bias, as high if at least one domain was at high risk of bias, or as unclear if at least one domain was at unclear risk of bias, and no domain was at high risk. This rule is specified by the Cochrane tool for assessing the risk of bias in randomized controlled trials because any source of bias in a trial is problematic, and there is a paucity of empirical research to prioritize one domain over the other.

3. Results

The initial search resulted in 5126 patents found with the term “Camellia sinensis” in the intellectual property banks selected, followed by the stage title and abstract read targeting dental applications from the first patent deposited until the last one that had a total of 28 patent registrations. Then, the repeated records (8) were deleted. At the end of the search, data and information from 20 selected patents were extracted (Table 1).

According to the searches, the United States Patent and Trademark Office (USPTO) and World Intellectual Property Organization (WIPO) were the banks with the largest number of filing patents for products/formulations with C. sinensis for dental applications with 7 (35%) and 6 (30%) patent registrations, respectively. The German Patent and Trade Mark Office (DPMA), Japanese Patent Office (JPO), and Swiss Federal Institute of Intellectual Property (IGE-IPI) did not provide patents related to the search.

Figure 1 shows the annual evolution of patent filings according to the number of patent registrations. There is an increase in the number of deposits, with a highlight from 2005 to 2006 with a total of 6 patents, also in 2016 with 3 registrations, and no deposits were found between 2017 and 2019. It is noteworthy that as expected in the last 18 months, the number of patents submitted found in the search is less than reality since many deposits are still in the period of confidentiality.

Figure 2 shows the origin of the patent applicants with a wide variety of countries, highlighting the United States as the largest applicant with 8 (40%), followed by South Korea with 4 (20%) and Brazil with 2 (10%) patent filings. Other countries, such as the United Kingdom, Italy, Germany, India, China, and Japan had only one patent registration, representing 5% each.

There were different types of patent applicants according to the findings. We observed that half of the patents filed (10) were inventions developed and registered by companies and industries. Also, the Colgate–Palmolive Company (US) showed most patents with three filings and the others with only one registration, among them the Nippon Zettoc Company, Ltd. (JP), Indena SpA Company (IT), and Amorepacific Corporation (KR). As well as, the applicants were represented by universities and research institutes with seven filings, among them Kingston University (UK), São Paulo University (BR), and Georgia Health Sciences University Research Institute (US). The other patents (3) had their applicants represented by people (inventor) and researchers.

In Figure 3, there is the distribution of classification of patented products indicating that the patent filings are more focused on human need section (A), and the classification A61K presented the largest number of patents (19), a category which includes patents for the preparations for medical, dental, or hygienic purposes, followed by A61Q with specific therapeutic activity of chemical compounds or medicinal preparations (7), and A01N with preservation of organisms of humans or animals or plants or their parts (3). As we can observe, some reports have more than one classification.

Figure 4 shows that the types of patented dental products with the term “Camelia sinensis” were the largest in composition form with 14 filings, and the remainder of the formulations is represented in mouthwash (3), toothpaste (2), and bagged tea (1). As for clinical application, 18 patents were filed as products with antimicrobial and antibiofilm action, while two patents are directed to the treatment of xerostomia.

Figure 5 shows the level of evidence of clinical trials studies about the efficacy of these formulations, found in the PubMed database. For the risk of bias, factors are random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. In general, the risk of bias of the studies was low, reinforcing that the formulations were effective.

4. Discussion

In the last decades, the scientific community and industries have shown a growing interest regarding the technological innovation for new products in dentistry, mainly based on the development of patents as intellectual property, which is a response to market demands [20]. Many of these inventions have been developed using natural products, such as C. sinensis extract, with different potential benefits for human oral health. Formulations containing C. sinensis in its composition look for advantages for treatment of oral
<table>
<thead>
<tr>
<th>Title</th>
<th>Publication number</th>
<th>Product</th>
<th>Country</th>
<th>Year</th>
<th>Classification IPC</th>
<th>Inventor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral composition comprising <em>Camellia</em> extract of semioxidized tissue from a member of the genus <em>Camellia</em> and an enhancing agent</td>
<td>2387/KOLNP/2009</td>
<td>Composition</td>
<td>UK</td>
<td>2006</td>
<td>A01N</td>
<td>Kingston University</td>
</tr>
<tr>
<td>Composição de higiene oral, método de tratamento ou prevenção de xerostomia e uso de polifenol de chá verde (gtp) (in Portuguese)</td>
<td>BRPI1008380</td>
<td>Composition</td>
<td>US</td>
<td>2008</td>
<td>A01N/A61K</td>
<td>Georgia Health Sciences University Research Institute, Inc.</td>
</tr>
<tr>
<td>Formulação tópica de uso bucal e seu uso (in Portuguese)</td>
<td>BR102016237505</td>
<td>Composition</td>
<td>BR</td>
<td>2016</td>
<td>A61K/A61P</td>
<td>University of São Paulo</td>
</tr>
<tr>
<td>Oral care compositions containing inibidores de metaloproteinases e seus usos (in Portuguese)</td>
<td>PI 1003771.3</td>
<td>Composition</td>
<td>BR</td>
<td>2010</td>
<td>A61K/A61Q</td>
<td>University of São Paulo</td>
</tr>
<tr>
<td>Oral care compositions for treating xerostomia</td>
<td>PCT/US2010/024906</td>
<td>Composition</td>
<td>US</td>
<td>2009</td>
<td>A01N/A61K</td>
<td>University of São Paulo</td>
</tr>
<tr>
<td>Compositions for the treatment and prevention of infections of the oral cavity</td>
<td>PCT/EP2009/002515</td>
<td>Composition</td>
<td>IT</td>
<td>2009</td>
<td>A61K/A61P</td>
<td>Indena SpA Company</td>
</tr>
<tr>
<td>Non-carious material and anticarious agent containing rare sugar</td>
<td>US 20100166678 A1</td>
<td>Composition</td>
<td>JP</td>
<td>2006</td>
<td>A61K/A61P</td>
<td>Matsutani Chemical Industry Co., Ltd./National University Corporation Kagawa University</td>
</tr>
<tr>
<td>Epigallocatechin-3-gallate crystal compositions</td>
<td>WO2008/153938</td>
<td>Composition</td>
<td>US</td>
<td>2007</td>
<td>C09K/A61P/C07D/A61K</td>
<td>University of South Florida The Procter &amp; Gamble Company</td>
</tr>
<tr>
<td>Oral care compositions combining combinations of antibacterial and host-response modulating agents Use of a phenol-containing extract from <em>Camellia sinensis</em> oral and dental cleaning agents for improving the visual appearance of the gums</td>
<td>US 2007/0053849 A1</td>
<td>Composition</td>
<td>US</td>
<td>2006</td>
<td>A61K/A61P/A61Q</td>
<td>Henkel Ag &amp; Co., KGaA</td>
</tr>
<tr>
<td>Oral composition containing saponin extracted from the root of <em>Camellia sinensis</em> for effectively preventing or treating periodontal diseases</td>
<td>WO/2016/062449</td>
<td>Composition</td>
<td>DE</td>
<td>2016</td>
<td>A61K/A61Q</td>
<td>Jeong Kee Kim; Su Kyung Kim; Dae Bang Seo; Seok Sik Moon Dongguk University Gyeongju Campus Industry-Academy Cooperation Foundation</td>
</tr>
<tr>
<td>Composition for enhancing oral hygiene comprising natural extract as active ingredient and use thereof</td>
<td>KR1020130035323</td>
<td>Composition</td>
<td>KR</td>
<td>2013</td>
<td>A61K/A61Q/Y10S</td>
<td>Eric M. Sanders</td>
</tr>
<tr>
<td>Health care buccal bag for refreshing mouth smell</td>
<td>CN10001586</td>
<td>Bagged tea</td>
<td>CN</td>
<td>2007</td>
<td>A61K/A61Q/A61P/A23F</td>
<td>Zhu Huagang</td>
</tr>
</tbody>
</table>
biofilm, helps promote the enamel and dentin remineralization by the fluoride component, and bad breath treatment [3, 6, 7, 12, 13, 15, 18].

Two reviews highlight and discuss patents that used *C. sinensis* and its derivatives for different applications according to the available literature. The first review highlighted that several patents were developed to improve tea processing methods for different purposes, including promoting changes in the composition of tea products, improving their sensory properties and stability, and increasing production yield [15]. The second reported invention patents using trihydroxybenzoate derivatives present in the tea composition of *C. sinensis* with antiviral, antifungal, and antibacterial properties related to different diseases, not only to oral health [14]. However, our study highlights recent patents that employed *C. sinensis* in formulations focused exclusively on dental applications, being the first review of patents for oral care on this topic.

The present study observed that the majority of patent deposits with *C. sinensis* belonged to the United States, both as an applicant country and as an intellectual property bank. Therefore, following the ranking of the WIPO statistical base, that when considering the technology areas, the United States is in first place in the medical field with patent...
deposits, including value-added dental equipment in the economic sector [24]. Among the types of applicants, the Colgate–Palmolive company was already expected to hold of a greater number of deposits, although the amount is not yet significant. Today, it represents a pioneering brand in the production of toothpaste, founded in New York (US) with more than 200 years of existence in the global market and later started to add the soap brand Palmolive.

The first patent registration (PI0519427-0) [25] entitled “Oral composition and methods for promoting the oral health of an animal patient, and for reducing the extension of discoloration in a toothpaste” was deposited in 2004 at the intellectual property bank Espacenet by the Colgate–Palmolive Company. The invention describes low water content toothpaste containing a variety of plant extracts, including C. sinensis, humectants, and abrasive compounds, together with an additional antioxidant component. Also, it proves methods for promoting the oral health of an animal patient.

In 2010, Buzalaf et al. [26] developed a BR patent (PI 1003771–3 A2) filed by the University of São Paulo for dental compositions (gel and/or varnish) containing metalloproteinase inhibitors, such as epigallocatechin-3-galate (EGCC) obtained from C. sinensis to be applied in the demineralization of the dental surface, caused by tooth decay or noncarious lesions, as well as preventing the progression of periodontal disease. More recently, in 2020, Juhwan Bio.Cell Company patented a foamable mouthwash solid formulation (WO/2020/054996) [27] which comprises a mixture of green tea and other extracts as an active ingredient. The inventors concluded that the product exhibits an excellent effect on dentin remineralization and dentinal tubule occlusion. Also, the invention has anti-inflammatory, antibacterial, dental caries-preventing, halitosis-eliminating, and scaling effects.

The consumption of C. sinensis is a promising agent in maintaining oral health, especially in relation to periodontal disease and caries [1, 7]. Its benefits concerning the prevention of dental caries are due to the leaves being accumulators of fluorine, with antimicrobial action, and the catechins (polyphenols) present have a protective effect on the dental tissue [1, 9, 12, 28]. In addition, the use of C. sinensis products for halitosis treatment suggests that this clinical condition can also benefit from these formulations. This fact is due to catechins capable of chemically reacting with sulfur compounds that promote bad breath, through a methylation reaction with orthoquinone, decreasing volatility, and neutralizing the chemical compound, and the antimicrobial activity decreasing the fermentation of sulfur compounds [7, 29]. There is also evidence that these polyphenolic catechins are active in preventing oral cancer and reducing bleeding after tooth extraction [7, 28, 30].

Mouthwash formulations stood out in the present study as a strategy for oral care because of their antimicrobial and anti-inflammatory properties, both in relation to patents and clinical trials found. Radafshar et al. observed the effects of a mouthwash containing 1% green tea tannins on dental biofilm and chronic gingivitis, comparing chlorhexidine and finding similar results [31]. Another clinical trial verified the effect of C. sinensis 5% mouthwash on gingivitis induced by biofilm accumulation for five weeks, observing positive effects and no adverse effects [32]. Sarin et al. also evaluated the effectiveness of a mouthwash containing 2% green tea compared to a placebo mouthwash for controlling plaque and gingivitis for four weeks, noting a significant reduction in plaque and gingival index in the group treated with C. sinensis mouthwash compared to placebo [33]. Another clinical trial evaluated the effectiveness of a mouthwash with 5% green tea to control pain and trismus associated with acute pericoronitis and compared it to the mouthwash with chlorhexidine, obtaining better results than the same [34]. According to Ardakani et al., C. sinensis becomes an alternative to a therapeutic agent carried in mouthwash, given that it has several other therapeutic properties differently from chlorhexidine [35].

![Figure 5: Review authors’ judgements about each risk of bias item presented as percentages across all included clinical studies.](image-url)
In a recent systematic review published, it was found that there is clinical evidence and a favorable safety profile for the use of *Camellia sinensis* in the form of mouthwash; these formulations are being able to act as antiseptic, antibiofilm, and anti-inflammatory agents. Thus, *Camellia sinensis* has a favorable phytochemical and pharmacological profile, making it a promising incorporation agent in mouthwashes [3]. These findings justify the highlight of the rinsing formulations in this view.

In view of all these therapeutic benefits of the constituents of *Camellia sinensis*, despite the small number of patents, it appears that this natural product has great potential for incorporation in dental products for oral care, which can be an attractive cost-effective alternative for consumers.

### 5. Conclusions

The study pointed out a small number of products protected by patents for *Camellia sinensis* for oral care indication, highlighting compositions to be incorporated in formulations, mainly mouthwash. In the methodological parameters of clinical trials carried out with the formulations, the majority pointed out a low risk of bias.

### Data Availability

This study used data available in the banks on intellectual property cited on the methods.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

### References


[25] M. Prencipe and E. S. Arvanitidou, "Colgate-palmolive company composição oral, e, métodos para a promoção de
saudé oral de um paciente animal, e para a redução da extensão de descoloração em uma pasta de dentes,” 2004.


