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Medicinal *Cannabis* in dentistry: a literature review

https://doi.org/10.32712/2446-4775.2026.2011

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Abstract

Contemporary dentistry faces recurring challenges in managing pain, modulating inflammation, and promoting tissue regeneration, especially in orofacial pain, periodontal diseases, and temporomandibular disorders. In this context, *Cannabis sativa* L. stands out as a promising medicinal ally. Historically used for multiple purposes, *C. sativa* L. was recently included in the Brazilian Common Denominations (DCB) list by Anvisa, legitimizing its therapeutic use in Brazil. Recent scientific advances have elucidated its mechanisms of action and primary phytocannabinoids, such as cannabidiol (CBD) and tetrahydrocannabinol (THC). These substances interact directly with the endocannabinoid system (ECS), a key biological regulatory system. Notably, endocannabinoid receptors have been identified throughout the oral cavity, including the oral mucosa, dental pulp, periodontal tissues, salivary glands, and temporomandibular joints. Activation of the ECS in these structures offers new perspectives for effective dental approaches by providing targeted analgesia, inflammation control, and antimicrobial effects. Consequently, integrating cannabinoids into dental practice represents a significant path toward improving clinical outcomes and enhancing patients' quality of life during treatments.

Keywords: medicinal cannabis; dentistry; orofacial pain; bruxism; burning mouth syndrome; oral mucositis.

Introduction

Cannabis is believed to have originated in Central Asia, with evidence of its use dating back over 12,000 years. It later spread to the Middle East, Africa, Europe, and the Americas[1].

In medicine, cannabis has been used for millennia to treat a variety of conditions, including pain, inflammation, mental disorders, and gastrointestinal problems. The first recorded medicinal use of cannabis dates back 3,500 years in what is now Romania[2]. Early evidence suggests cannabis may have been used for pain relief as early as 400 A.D.[2]. The plant was first listed as a medicinal product in the United States Pharmacopeia in 1850[2].

In the 1970s, Brazilian scientist and professor at the Escola Paulista de Medicina, Elisaldo Carlini, demonstrated the anticonvulsant potential of cannabinoids[3]. Bulgarian professor Raphael Mechoulam collaborated on this and other studies and is therefore considered the "father of endocannabinoid science"[4].

Although medicinal cannabis has been used therapeutically for thousands of years, in recent decades it has gained increasing attention across various fields due to its therapeutic potential in numerous areas of health[5-7].

Phytocannabinoids, also known as classical cannabinoids, are a class of terpenophenolic compounds biosynthesized by the *Cannabis sativa* L. plant. More than a hundred phytocannabinoids have now been isolated from this species, with Δ9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) being the most studied and most concentrated in different plant varieties. Other identified bioactive molecules include tetrahydrocannabivarin (THCV), cannabigerol (CBG), cannabichromene (CBC), cannabivarin (CBV), cannabicyclol (CBL), cannabigerovarin (CBGV), cannabichromene varin (CBCV), and cannabidivarin (CBDV), all of which belong to the group of secondary metabolites[8].

Secondary metabolites are organic substances produced by plants and microorganisms which, although not essential for cellular physiology, confer adaptive advantages such as protection from predators, resistance to environmental stresses, and attraction of pollinators. In the context of *Cannabis sativa* L., beyond phytocannabinoids, other secondary metabolites also stand out for their relevant pharmacological properties, including flavonoids and terpenes. The latter are responsible for the plant's organoleptic characteristics—aroma, flavor, and pigmentation - while also contributing therapeutic effects[9,10].

Among the terpenes most frequently identified in *C. sativa* L. are limonene, caryophyllene, humulene, and myrcene, all of which possess anti-inflammatory, analgesic, antioxidant, anxiolytic, and immunomodulatory properties[10]. The synergistic interaction between phytocannabinoids and other metabolites, including flavonoids and terpenes, enhances the plant's pharmacological effects - a phenomenon known as the "entourage effect"[10]. This synergy gives *C. sativa* L. extracts an amplified therapeutic potential, with possible applications in dentistry, especially in the management of inflammatory, painful, or infectious oral conditions[10]. Thus, phytocannabinoids and their adjunct compounds emerge as promising candidates in the development of therapeutic strategies aimed at oral and dental health.

This article aims to conduct a literature review on the use of medicinal cannabis in dentistry, addressing its benefits, mechanisms of action, and potential adverse effects.

Regulatory Overview

Regulations regarding the use of medicinal cannabis vary significantly between countries. In Brazil, therapeutic use is authorized under the regulations of ANVISA. Cannabis-based products can be prescribed by both physicians and dentists; however, recreational use remains prohibited. According to ANVISA's

Collegiate Board Resolution (RDC) nº. 660/2022[11], the importation of cannabis-based products is permitted with proper authorization. Although RDC nº. 1015/2026[12] does not explicitly mention prescription by dentists, Ordinance nº. 344/1998[13] approves the technical regulations concerning substances and medications subject to special control, recognizing dentists as authorized prescribers of cannabis for medicinal purposes. Cannabis cultivation may be authorized for companies with medical and industrial purposes, but not for personal use.

In the United States, medicinal cannabis is legal in more than 30 states, each with its own specific regulations. Cultivation is also permitted in states where either medicinal or recreational use is legal[14]. In Canada, both medicinal and recreational use have been legal since 2018, with cultivation allowed for both personal and commercial purposes[15]. In Europe, each country has its own policy. Germany had already legalized medicinal use and, in 2024, also legalized recreational use. In the United Kingdom, recreational use remains prohibited, while therapeutic use is legal. In the Netherlands, consumption is decriminalized, but sales are restricted to specialized establishments known as coffee shops[16]. In other South American countries - Argentina, Colombia, Chile, Peru, and Paraguay - medicinal use is permitted. Uruguay was the first country in the world to fully legalize cannabis for both medicinal and recreational purposes, including authorization for personal and commercial cultivation[17,18].

Justification for the Literature Review

In recent years, scientific and clinical interest in medicinal cannabis has grown significantly, driven by regulatory advances, new discoveries regarding the endocannabinoid system, and promising reports of its therapeutic applications. Several studies highlight its potential in managing chronic pain, inflammation, neurological and psychiatric disorders, as well as its usefulness in dentistry, particularly in controlling orofacial pain and inflammatory processes. The growing number of prescriptions for cannabis-based treatments, especially in cases refractory to conventional therapies or those that are difficult to manage, has contributed to this increasing interest[19].

However, despite the growing body of research, gaps remain in the literature concerning the efficacy, safety, and mechanisms of action of medicinal cannabis for different dental conditions[20-22]. Many studies present methodological limitations, inconsistencies in cannabinoid concentrations, and a lack of standardization in administration routes, which hinder the translation of scientific findings into clinical practice.

Given this context, a literature review becomes essential to gather and critically analyze the available evidence, highlighting advances, challenges, and future perspectives regarding the use of medicinal cannabis. Such an approach helps identify patterns, suggest directions for new research, and support evidence-based decision-making in both clinical practice and public policy formulation. Considering the limited evidence assessing the effects of cannabis-based products in dental practice, the authors believe that a broader discussion on the subject would be of interest to the readers.

Therefore, this study aimed to analyze the recent literature on the use of medicinal cannabis in dentistry, emphasizing its main therapeutic applications, safety, and regulatory aspects. The review seeks to compile and critically assess the available scientific evidence, focusing on the potential of cannabinoids in managing orofacial pain, inflammation, and other dental conditions. Additionally, it aims to discuss the challenges

Revista Fitos. Rio de Janeiro. 2026; 20(1): e2011 | e-ISSN: 2446-4775 | www.revistafitos.far.fiocruz.br |

related to standardization, adverse effects, and regulation, offering a comprehensive overview that can support clinical practice, public policy development, and future research in the field.

Methodology

A narrative literature review was conducted using the PubMed, SciElo, and Cochrane databases, covering the period from 2000 to 2025. The search terms included: "medicinal cannabis", "dentistry", "orofacial pain treatment", "bruxism", "gingival and periodontal diseases", "oral inflammation", "burning mouth syndrome", "mucositis", and "anti-inflammatory action of cannabis", in both English and Portuguese. The selected articles were assessed based on methodological quality and clinical relevance.

Inclusion and Exclusion Criteria

The inclusion criteria comprised clinical and preclinical studies on the use of medicinal cannabis in various dental treatments published between 2000 and 2025, in English or Portuguese, and peer-reviewed publications. Articles without full-text access, studies not directly related to dentistry, publications focusing solely on recreational cannabis use, and articles that did not address the efficacy or safety of medicinal cannabis were excluded from this review.

Results and Discussion

Using the search descriptors mentioned above, a total of 135 articles were initially found in the PubMed, SciELO, LILACS, and Scopus databases. After reviewing titles and abstracts, 32 articles were excluded for not directly addressing the application of medicinal cannabis in the dental context or for being duplicates across databases. This left 103 articles for full-text review, of which 44 were excluded for not meeting the predefined inclusion criteria, such as a specific focus on the dental field, clinical relevance, and publication between 2000 and 2025. Thus, 59 articles were selected to compose the present study, providing theoretical and scientific support on the potential therapeutic uses of medicinal cannabis in dentistry.

This review identified relevant studies indicating that medicinal cannabis may be effective in relieving orofacial pain, reducing gingival inflammation, and treating hard-to-manage conditions such as temporomandibular disorders, among others (**TABLE 1**). Although current data are promising, the application of medicinal cannabis in dentistry still requires further randomized controlled trials to more robustly confirm its efficacy and safety. Continued research and the development of specific clinical guidelines will be essential for integrating this therapy into dental practice.

The regulation of medicinal cannabis also has a significant impact on public health, as it enables access to treatments that may be effective in managing difficult dental conditions such as orofacial pain, refractory periodontal diseases, burning mouth syndrome, bruxism, dental anxiety, and overall improvements in quality of life especially in debilitating conditions. However, the lack of adequate regulation can lead to inequalities in access to treatment, favoring only those who can afford expensive products. It may also place additional pressure on the public health system due to legal proceedings, as patients increasingly turn to the judiciary to obtain cannabis-based treatments.

Revista Fitos. Rio de Janeiro. 2026; 20(1): e2011 | e-ISSN: 2446-4775 | www.revistafitos.far.fiocruz.br |

Furthermore, other obstacles must be addressed to expand the availability of cannabis-based therapies. These include the lack of standardization in cannabis use and dosing, given the absence of protocols due to the individuality of each person's endocannabinoid system; the need for constant patient monitoring, especially during dosage titration; and the necessity for a personalized, non-standardized approach to treatment. These factors alongside the need for more robust clinical studies and the high cost of cannabis-derived medications represent challenges that must be overcome to ensure broader and equitable access to this form of therapy.

TABLE 1: Summary of key studies and outcomes related to medicinal cannabis in dentistry.

Year	Authors	Article	Magazine	Type of study	Country of origin	Study area	Main outcome
2014	McDonough P, *et al.*	Neuropathic orofacial pain: Cannabinoids as a therapeutic avenue	Int. Journal of Biochemistry & Cell Biology	Literature review	UK/ Ireland	Neuropathic orofacial pain; Trigeminal neuralgia	Chronic neuropathic pain (NOP) often cannot be satisfactorily treated with conventional analgesics, therefore alternative treatment options are sought. Cannabinoids actively target many pathophysiological mechanism that contribute to NOP disorders, cannabinoids such as Sativex may represent a genuine therapeutic strategy for these conditions
2017	Konermann A, *et al.*	In vivo and *in vitro* identification of endocannabinoid signaling in periodontal tissues and their potential role in local pathophysiology	Cellular and Molecular Neurobiology	In vivo and In vitro analysis	United States/ Germany	Periodontology	CB1 and CB2 are the two receptors of the endocannabinoid system (ECS) that are expressed in periodontal tissues with distinct expression changes in different inflammatory conditions. The existence of CB1 in non-neuronal tissues sheds new light on the localization and function of the CB receptor, adding a new dimension to the complexity of ECS regulation within the body.
2024	Walczynska-Dragon, *et al.*	Cannabidiol intervention for muscular tension, pain, and sleep bruxism intensity - a randomized, double, blind clinical trial.	Journal of Clinical Medicine	Double-blind randomized clinical trial	Switzerland/ Poland	Bruxism, Orofacial pain and temporomandibular dysfunction (TMD)	Intraoral use of CBD reduced pain, muscular tension, and bruxism intensity; 10% CBD concentration was superior to 5%.
2024	Grossmann E, *et al.*	The current state of cannabinoids in orofacial pain	Clinics Editorial	Editorial	Brazil	Orofacial pain	The endocannabinoid system offers a promising target for cannabinoid-based interventions. Current research suggests that cannabinoids, particulary when used in combination with other treatments, may provide relief for patients suffering from chronic orofacial pain.
2023	Tambeli CH, *et al.*	Integrative approach to the therapeutic use of cannabis in orofacial pain	Brazilian Journal of Pain	Literature review	Brazil	Orofacial pain	Cannabinoid therapy is part of an integrative approach that improves therapeutic outcomes and quality of life.
2016	Gajofatto A.	Refractory trigeminal neuralgia responsive to nabiximols in a patient with multiple sclerosis.	Multiple Sclerosis and Related Disorders	Case study	United Kingdom/ Italy	Trigeminal neuralgia; Multiple sclerosis	After starting treatment with nabiximols, the patient showed significant benefit in trigeminal neuralgia, which was completely resolved, while spasticity

Year	Authors	Article	Magazine	Type of study	Country of origin	Study area	Main outcome
							responded only partially to treatment. Nabiximols and other cannabinoids need further testing for the treatment of trigeminal neuralgia.
2019	Nitecka-Buchta A, *et al.*	Myorelaxant effect of transdermal cannabidiol application.	Journal of Clinical Medicine	Double-blind randomized clinical trial	Switzerland/ Poland	Bruxism and TMD	Transdermal application of CBD on the masseter muscle reduced its activity and improved the condition of masticatory muscles in patients with myofascial pain.
2023	Carmona Rendón Y, *et al.*	Cannabinoids in periodontology: Where are we now?	Antibiotics	Literature review	Switzerland/ Colombia	Periodontology	Analysis of the endocannabinoid system and the physiological impacts of cannabinoids on the periodontium revealed immunomodulatory and antibacterial properties, potentially contributing to adequate healing and regeneration of periodontal tissues. Although more evidence is needed, current data support ongoing research on these agents as a viable option for therapeutic interventions in periodontics.
2023	Pellegrini G, *et al.*	Involvement of the endocannabinoid system in current and recurrent periodontitis: A human study.	Journal of Periodontal Research	Clinical trial	Denmark/ Italy	Periodontology	The endocannabinoid system appears to be involved differently in individuals with recurrent and non-recurrent periodontal disease.
2020	Stahl V, Vasudevan K.	Comparison of efficacy of cannabinoids versus commercial oral care products in reducing bacterial content fron dental plaque: a preliminary observation.	Cureus	Clinical trial	United States/ Belgium	Periodontology	Cannabinoids have the potential to be used as an effective antibacterial agent against plaque-associated bacteria. Furthermore, they were more effective in reducing bacterial colony counts in dental plaque compared to products such as Oral B and Colgate.
2020	Vasudevan K, Stahl V.	Cannabinoids infused mouthwash products are as effective as chlorhexidine on inhibition of total-culturable bacterial content in dental plaque samples.	Journal of Cannabis Research	Randomized clinical trial	Germany/ Belgium	Periodontology	Cannabinoid (CBD/CBG) infused mouthwashes, along with other essential natural ingredients, show promising in vitro bacterial activity against aerobic bacterial content in dental plaque, with efficiency equivalent to or greater than the gold standard (0.2% chlorhexidine).
2014	Borsani E, *et al.*	Epithelial expression of vanilloid and cannabinoid receptors: a potential role in burning mouth syndrome pathogenesis.	Histology and Histopathology	Clinical trial	Spain	Burning Mouth Syndrome (BMS)	In patients with BMS, there was an increase in TRPV1 expressions, a decrease in CB1 expression and an increase in CB2 expression in the epithelial cells of the tongue, also associated with an alteration in their distribution. It seems that these receptors are related to BMS. These data may be useful for the future characterization of epithelial markers and therapy of BMS.

Year	Authors	Article	Magazine	Type of study	Country of origin	Study area	Main outcome
2022	Pereira SR, *et al.*	Recent advances in the understanding of the aetiology and therapeutic strategies in burning mouth syndrome: focus on the actions of cannabinoids	European Journal of Neuroscience	Literature review	United Kingdom	Burning Mouth Syndrome (BMS)	This review identifies cannabinoid-based therapeutics for consideration in the management/treatment of BMS. Given the known neuroprotective, anti-inflammatory, antioxidant, and antiapoptotic properties of cannabinoids, a thorough investigation of the cannabinoid system as a reliable therapeutic strategy in BMS is warranted.
2024	Yang J, *et al.*	Cannabidiol alleviates oral mucositis by inhibiting PI3K/Akt/NF-κB-mediated pyroptosis.	Balkan Medical Journal	Preclinical experimental study	Turkey/ China	Oral Mucositis	Findings suggest a novel mechanism for the control of oral mucositis (OM), in which CBD suppresses the PI3K/ Akt /NF- kB signaling pathway and pyroptosis, thereby attenuating the symptoms of OM.
2023	Umpreecha C, *et al.*	Efficacy and safety of topical 0.1% cannabidiol for managing recurrent aphthous ulcers: a randomized controlled trial.	BMC Complementary Medicine	Randomized clinical trial	Germany	Recurrent Aphthous Stomatitis	Topical use of 0.1% CBD reduced the size of ulcers and accelerated healing without side effects.
2021	Lowe H, *et al.*	The Current and potential application of medicinal cannabis products in dentistry	Dentistry Journal	Literature review	Switzerland	General Dentistry (dental pain, periodontology, mourning mouth syndrome, dental caries, dental anxiety, mucositis, oral cancer)	Cannabinoids have applicability in dentistry for the treatment of (1) tooth pain, (2) bacterial infections causing periodontitis, gingivitis, periodontal disease, dental caries, salivary gland infections and abscesses, (3) inflammatory oral diseases, (4) oral and salivary gland cancers, (5) burning mouth syndrome, (6) dental anxiety, and (7) for general oral hygiene maintenance, and ab cavities, dental anxiety, and oral hygiene.
2023	Garcia JBS, Barbosa Neto JO.	Adverse effects of cannabinoid use: what is the safety paradigm?	Brazilian Journal of Psychiatry	Literature review	Brazil	Medicine/ General	Evidence regarding adverse effects is still contradictory and weak; more research is needed to elucidate safety.
2020	Gambino A, *et al.*	Evaluating the suitability and potential efficiency of cannabis sativa oil for patients with primary burning mouth syndrome: a prospective, openlabel, single -arm, pilot study.	Pain Medicine	Prospective single-arm open-label pilot study	United States/ Italy	Burning Mouth Syndrome (BMS)	In this pilot evaluation, the Cannabis sativa oil provided was effective and well tolerated in patients with BMS. However, larger, well-defined randomized clinical trials with different therapeutic approaches or placebo-controlled trials are needed.
2021	Grossman S, *et al.*	Cannabis and orofacial pain: a systematic review	British Journal of Oral and Maxillofacial Surgery	Systematic review	UK	Orofacial pain	There is a paucity of literature on the effects of cannabis-based products on the orofacial region; however, there is some high-quality evidence supporting their use in the treatment of

Year	Authors	Article	Magazine	Type of study	Country of origin	Study area	Main outcome
							chronic nociceptive and neuropathic pain conditions. Further research is needed to explore and substantiate the therapeutic role of CBDs in the context of orofacial pain and inflammation.
2024	Santos RMM, *et al.*	Therapeutic use of cannabis on dentistry in the treatment of orofacial pain: integrative literature review	Brazilian Journal of Implantology and Health Sciences	Literature review	Brazil	Orofacial pain	Orofacial pain is among the most common situations in dental care, and the use of cannabis proves to be an important ally in the treatment of these discomforts, being able to enhance the action of medications already used in these treatments or even replacing them. However, there is a need for more studies to prove the safety of its use, adverse effects and drug interaction with other medications.
2010	Beneng K, *et al.*	Cannabinoid receptor CB1 immunoreactive nerve fibers in painful and non-painful human tooth pulp..	Journal of Clinical Neuroscience	Observational study	Netherlands/ England	Odontogenic pain	The CB1 receptor is expressed in nerve fibers of the human dental pulp, and dental pain may be a useful clinical model to advance the development of peripherally restricted CB1 agonists for the treatment of chronic pain.
2020	Boyaji S, *et al.*	The role of cannabidiol (CBD) in chronic pain management: as assessment of current evidence.	Current Pain and Headache Reports	Literature review	Germany/ United States	Chronic Pain	Cannabinoid-based medicines, especially CBD, are promising tools in the field of pain management.
2022	Tan HL, Smith JG, Hoffmann J, Renton T	A systematic review of treatment for patients with burning mouth syndrome	Cephalalgia	Systematic review	United Kingdom	Burning Mouth Syndrome	A larger sample size, multicenter, multiarm comparison of therapeutic agents with placebo, and longitudinal follow-up studies are recommended to establish a standardized treatment protocol for burning mouth syndrome.
2015	Ware MA, *et al.*	Cannabis for the management of pain: assessment of safety study (COMPASS).	The Journal of Pain	Prospective cohort study	Canada	Chronic pain	This study evaluated the safety of cannabis use in patients with chronic pain over 1 year. The study found a higher rate of adverse events among cannabis users compared with controls, but no serious adverse events at an average dose of 2.5g of cannabis per day.
2021	Sihota A, *et al.*	Consensus-based recommendations for titrating cannabinoids and tapering opioids for chronic pain control.	International Journal of Clinical, Practice	Consensus-based recommendations	Canada	Chronic pain	The five-step modified Deplhi process led to the development of consensus-based recommendations on the safe introductions and titration of cannabinoids in conjunction with opioid tapering.

Therapeutic Applications of Medicinal Cannabis in Dentistry

Chronic Pain / Orofacial Pain

Chronic orofacial pain, including temporomandibular disorders (TMD) and neuropathic pain, as well as chronic pain in general, is difficult to manage therapeutically. Pain is influenced by psychological, cognitive, behavioral, social, and neurophysiological factors[23]. Recognizing the biopsychosocial model of chronic pain makes clear the need for treatment with an integrative approach, aiming for the patient's health and well-being with a perspective that goes beyond somatic causes[4]. In most cases, chronic pain is treated with opioids (which may lead to drug abuse), antidepressants, and anticonvulsants. Due to the disadvantages of opioids, cannabis is being considered a useful treatment for pain, and its legalization in some countries has led to a decrease in deaths from opioid overdoses[24].

In this context, cannabinoids emerge as a possible therapeutic option[23]. Currently, there is consensus to consider cannabis for the treatment of neuropathic pain, inflammatory pain, and nociplastic pain[25]. Patients generally present to doctors and dentists with various etiologies of orofacial pain, including acute pain (for example, pulpitis, apical periodontitis, postoperative surgical pain), chronic pain conditions (for example, temporomandibular joint disorders (TMD), including myogenic and arthrogenic pain), and neuropathic pain (for example, trigeminal neuralgia, burning mouth syndrome), among others[26].

The mechanism of cannabinoids occurs through activation of two predominant receptors, cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2)[26]. There is extensive literature supporting the presence of cannabinoid receptors and ligands (CB) in the central and peripheral nervous systems and in other tissues, such as bone and within the immune system[27]. Additionally, CB receptor expression has been observed in dental pulp[26] and periodontal tissues[28].

One study investigated the action of phytocannabinoids in the treatment of neuropathic orofacial pain such as trigeminal neuralgia, persistent idiopathic facial pain, burning mouth syndrome, and post-herpetic neuralgia. The authors concluded that cannabinoids have a therapeutic effect in reducing pain perception, especially for these conditions[29]. A systematic review on the use of cannabis-based medications for orofacial pain control highlighted the need for more robust randomized controlled trials to establish clearer clinical guidelines[26]. Other studies have explored the therapeutic potential of cannabinoids in specific orofacial pain conditions such as trigeminal neuralgia and burning mouth syndrome (BMS). Trigeminal neuralgia, a severe form of facial pain, has shown good results with cannabis-based treatments such as nabiximols, which combines THC (tetrahydrocannabinol) and CBD in a spray formulation[30]. Meanwhile, Burning Mouth Syndrome (BMS), a chronic pain condition characterized by a burning sensation in the mouth, showed symptom reduction with cannabis sativa oil, further emphasizing the potential of cannabinoids in specific pain conditions[31,32].

Despite these promising developments, there are several barriers to the widespread use of cannabinoids in treating orofacial pain[30]. The legal and regulatory environment around cannabis and cannabis-based products varies widely between countries and even regions within countries. Additionally, the psychoactive effects of THC, particularly at higher doses, limit its acceptability for long-term use in certain patient populations[29].

Orofacial pain is among the most common conditions in dental care, and the use of cannabis appears to be an important ally in treating these discomforts, potentially enhancing the action of medications already used in these treatments or even replacing them[24]. However, more studies are needed to prove the safety of its use.

Bruxism and Temporomandibular Disorder (TMD)

The term "temporomandibular disorders" (TMDs) collectively refers to a group of musculoskeletal conditions affecting the temporomandibular region[33]. Pain associated with TMD is classified as acute or chronic, with patients frequently experiencing symptoms such as muscle pain, restricted mandibular movements, otologic symptoms, increased dental pain or sensitivity, headache, pain in the temporomandibular joint area, periorbital pain, and limited cervical movements. These clinical manifestations can significantly impact sleep patterns, quality of life, and psychological well-being of an individual[34-36]. Recurrent temporomandibular disorders (TMDs) related to muscles generally arise due to hyperactivity and overuse of the masticatory muscles, often triggered by bruxism, which is recognized as a contributing factor to various dental pathologies, including periodontal complications, dental and root fractures, prosthetic malfunction, and dental wear[33].

Bruxism has been categorized into two forms: sleep bruxism (SB) and awake bruxism (AB). Sleep bruxism involves masticatory muscle activity (MMA) during sleep, characterized by rhythmic (phasic) or non-rhythmic (tonic) patterns. In contrast, awake bruxism involves masticatory muscle activity during wakefulness, usually marked by repetitive or sustained dental contact and/or mandibular locking or thrusting[33].

The etiology of bruxism largely involves biological, psychological, and social factors, requiring a multifaceted treatment approach[34]. Over time, various therapeutic modalities have been suggested, some becoming obsolete while others have gained strength. However, due to the diversity of symptoms associated with TMDs, finding a universal treatment remains challenging[33].

Recent attention has been directed toward cannabidiol (CBD) as a potential adjuvant in relieving orofacial myofascial pain[35,36]. CBD is considered a regulator of many physiological processes, such as pain sensation and inflammation[37]. Despite limitations, significant evidence describes the therapeutic effects of CBD, including anticonvulsant, antipsychotic, chronic pain relief, muscle relaxation, anxiolytic, neuroprotective, and sleep-promoting effects[36,38]. In this context, this phytotherapeutic agent is responsible for inhibiting the synaptosomal reuptake of norepinephrine, dopamine, serotonin, and gamma-aminobutyric acid, as well as the reuptake of anandamide in cells. It also inhibits sodium and calcium channels, thus dampening nerve excitability, which may contribute to reducing pain hypersensitivity and seizures[34-36]. Researchers are increasingly exploring strategies to administer CBD to individuals suffering from temporomandibular disorders characterized by muscle hyperactivity or temporomandibular joint inflammation[34-36]. There is considerable evidence in the literature supporting the use of cannabis-based products to treat neuropathic and chronic nociceptive pain. However, the authors noted that evidence specifically related to orofacial symptoms is very limited[20]. The authors of the following randomized trial aimed to evaluate the effects of intraoral CBD gel application in reducing pain, bruxism index, and muscle activity in patients suffering from muscle-related TMDs[34].

In a randomized study, the authors investigated the impact of intraoral CBD use on muscle tension and pain correlated with bruxism and TMD[39]. The use of CBD formulations in patients with TMDs proved to be a successful treatment to reduce pain, muscle tension, and bruxism activity in individuals with sleep bruxism

and muscular TMD. Patients who received a higher concentration CBD formulation (10%) showed remarkable improvements in sensations of pain, muscle tension, and bruxism intensity compared to those who received the lower CBD concentration (5%). Interestingly, individuals who received placebo showed minimal changes in these parameters[39].

Another similar study explored the effects of CBD via extraoral application. In this doubleblind trial, a CBD formulation applied over the masseter muscles led to reduced muscle activity and also improved the condition of the masticatory muscles in patients with myofascial pain[39]. Despite variations in CBD concentrations, it can be concluded that the extraoral application produced more favorable results in terms of patient pain sensations. However, intraoral application demonstrated greater reductions in electromyography results and bruxism activity during sleep[39].

Periodontology

Periodontal disease is an inflammatory condition affecting the supporting tissues of the teeth, frequently associated with microbial dysbiosis and systemic implications that play a crucial role in its connection with multiple diseases[31,40,41].

A study detailed that patients with recurrent periodontitis showed higher levels of cannabinoid receptors (CB1 and CB2) in inflamed tissues and lower activation of these receptors compared to non-recurrent patients and healthy individuals[31,40,41].

In healthy individuals, CB1 and CB2 receptors were equally expressed, with no differences between epithelium and connective tissue. When inflammation occurs, both in recurrent and non-recurrent patients, the expression of these receptors resulted in upregulation, particularly in the superficial layers (granular and corneal layers) of the epithelium, which showed significantly higher receptor levels compared to connective tissue. These data confirm the involvement of CB1 and CB2, and the epithelium associated with periodontal inflammation[40,41].

Cannabinoid receptors seem to play a role in promoting periodontal tissue healing by enhancing fibroblast adhesion and migration and increasing osteo/dentinogenic differentiation of periodontal ligament stem cells, even during tissue inflammation[21,40,41]. Inflamed sites of recurrent patients showed significantly greater amounts of CBs than other groups. This much higher CB expression in inflamed sites of recurrent periodontal disease may indicate a greater susceptibility of the tissue to activate protective cellular/molecular mechanisms against periodontal destruction that follows bacterial infection[21,40,41].

In this context, phytocannabinoids have demonstrated remarkable antimicrobial properties against a variety of bacteria and fungi. It was found that cannabigerol (CBG) reduces *Streptococcus mutans* biofilm expression, inhibiting its formation at a minimum biofilm inhibitory concentration of 2.5 µg/mL and decreasing metabolic activity at higher concentrations (10 µg/mL). Similarly, CBD, cannabinol (CBN), and THC suppressed the growth of *Porphyromonas gingivalis* and *Filifactor alocis*, but *Treponema denticola* was resistant to all tested doses. THC also had a prebiotic effect, preserving comensal bacteria. The impact of THC on the microbiota was particularly notable[41,42].

Another study comparing the efficacy of cannabinoid-based oral hygiene products found that CBD surprisingly reduced bacterial colony density, similarly to other well-established oral hygiene formulations, with variations in effectiveness due to oral biofilm heterogeneity. It was also effective against Gram-positive

bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) strains, and inhibited *Streptococcus mutans* biofilm formation, which may also be important in caries prevention[41,42].

Cannabigerol (CBG), another cannabinoid present in the plant, also showed strong antimicrobial activity effective against both Gram-positive and Gram-negative bacteria, and significantly reduced biofilm formation and metabolic activity of *S. mutans* biofilms (maintenance)[21].

Mouthwashes are widely used during periodontal therapy as an aid in chemical plaque control. In this context, a study compared the efficacy of cannabinoid-containing mouthwashes (CBD, CBG) with already marketed oral hygiene products. Greater efficacy in reducing bacterial colonies was demonstrated with cannabinoids compared to marketed oral hygiene products. Phytocannabinoid-based mouthwashes (CBD, CBG) showed bactericidal efficiency equivalent or superior to 0.2% chlorhexidine (gold standard)[40,41].

Based on this evidence, it is suggested that agonists of these endocannabinoid system channel, such as THC and CBD, are promising alternatives for the effective treatment of periodontitis, although more controlled clinical studies are needed to consolidate this therapy[21].

Burning Mouth Syndrome

Burning Mouth Syndrome (BMS) is a chronic idiopathic orofacial pain condition, characterized by intraoral burning or dysesthesia recurring daily for more than 2 hours per day and for more than 3 months, without identifiable causative lesions[43]. Prevalence ranges from 0.1% to 3.9% and primarily affects postmenopausal women aged 50 to 70. Common symptoms include burning, “stinging,” tingling, itching, or numbness of the tongue, lips, palate, gums, and other oral mucosa. Pain intensity increases throughout the day, peaking late at night[44]. Patients with BMS experience a burning sensation on oral mucosal surfaces, frequently accompanied by xerostomia (dry mouth), dysgeusia (altered taste), tingling, or paresthesia-like sensations, but without clinically evidence causative lesions[44].

The etiology of BMS is not yet fully understood and is considered a multifactorial condition. Misclassification of the disorder complicates diagnosis, especially for clinicians and dentists. The numerous painful sensations of the oral mucosa may be explained by local or systemic pathologies affecting the oral cavity, such as nutritional deficiencies of vitamin B12, iron, zinc, or folic acid; use of certain medications such as corticosteroids, analgesics, antibiotics, estrogen, retinoids, benzodiazepines, and psychotropics; presence of systemic diseases like diabetes and Sjögren’s syndrome; erosive lesions; *Candida* spp. infection; damage induced by prosthesis use; and even presence of metallic compounds in the mouth, such as use of metal-ceramic crowns opposed to BMS[44].

Psychological and psychiatric disorders appear closely related to the pathogenic mechanisms of this oral manifestation, as they are prevalent in a significant number of BMS patients, contributing to a poor prognosis[44]. This multifactorial etiology, possibly associated with interaction of neuropathic, hormonal, psychological, and local factors, along with the variety of reported symptoms, challenges treatment, often leading to frustration and consequent abandonment of treatment[44,45].

An investigation inferred that BMS generally develops in postmenopausal women. Nagamine[46] suggests that fluctuations in estrogen levels throughout life may play a crucial role in BMS development by modulating the transient receptor potential vanilloid 1 (TRPV1) receptor and nerve growth factor (NGF). Increased

estrogen at puberty could sensitize individuals, while decreased estrogen at menopause could trigger BMS, leading to increased NGF and TRPV1 expression on the cell surface. However, further research with larger samples, multicenter studies, and longitudinal follow-up are necessary to establish standardized treatment protocols and to validate the estrogen theory in BMS development[47].

Other experimental studies showed altered expression of TRPV1, CB1, and CB2 receptors in epithelial cells of the tongue in BMS patients[48]. The presence of CB1 and CB2 receptors in the mouth and altered expression of these receptors in the tongues of BMS patients suggest the endocannabinoid system may be a therapeutic target. The classical G protein-coupled cannabinoid receptor (CB1) is downregulated in the tongue epithelium of BMS patients, while cannabinoid receptor-2 (CB2) and transient receptor potential vanilloid 1 (TRPV1) receptors are upregulated[44,49]. Although the etiology of the disease is unknown, these findings contribute to better elucidation of mechanisms involved in its treatment, suggesting CBD, an agonist of TRPV1 and CB1/CB2 receptors, as an alternative to modulate nociception and other symptoms such as anxiety and stress related to the condition[22,46,48].

Cannabis sativa and its cannabinoid constituents have been the focus of extensive biomedical research[50]. A pilot study showed that *C. sativa* oil was effective and well tolerated in 17 patients with primary BMS, with subjects showing improvement over time in terms of clinical remission of oral symptoms[50]. Anxiety and depression levels also showed favorable improvement. In the mentioned pilot study, using a whole-plant cannabis extract diluted in olive oil, patients showed significant pain intensity improvement at the end of the 4-week protocol and during the following 24 weeks. No serious adverse effects were reported and no patient had to discontinue treatment[31,50].

Although preliminary, the results suggest CBD may be an effective alternative for BMS treatment, especially in patients unresponsive to conventional therapies. However, the authors emphasized the need for larger, better-defined randomized controlled clinical trials with different therapeutic approaches or placebo control to confirm these results. This study was pioneering in analyzing the role of cannabinoids in treatment of refractory BMS. The formulation with similar concentrations of THC and CBD appeared to provide immediate pain relief, with a delayed anxiolytic effect possibly related to pain reduction[47,49,50].

Oral Mucositis

Oral mucositis is an acute inflammatory condition of the oral mucosa associated with chemotherapy and radiotherapy in oncology patients. It is characterized by intense pain, erythema, ulceration, and impairment of oral function, which negatively impacts quality of life and can lead to interruption of antineoplastic treatment[51]. The pathophysiology of mucositis involves a cascade of inflammatory events, oxidative stress, and release of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6[41,50,52].

Given the limited effective and safe therapies for mucositis management, despite considerable economic costs due to hospitalizations and clinical implications ranging from patient malnutrition to dehydration, no effective therapy has been developed so far[41,45]. Thus, there is growing interest in the therapeutic use of phytocannabinoids, especially cannabidiol (CBD) and THC, which demonstrate anti-inflammatory, analgesic, antioxidant, and immunomodulatory properties[53]. For example, CBD inhibits the production of inflammatory cytokines and reduces oxidative stress, potentially attenuating the pathological processes

involved in this condition[54]. Meanwhile, THC, besides modulating pain via CB1 receptors, may exert anti-inflammatory effects through activation of CB2 receptors in the imune system[45].

Preclinical and clinical studies have been investigating the topical and systemic application of cannabinoids for pain control, inflammation reduction, and acceleration of oral mucosa healing[45,50,51]. Topical administration via orabase-type gels or mouthwashes containing CBD or *Cannabis sativa* L. extracts has shown promise, with significant pain reduction and shortened recovery time, along with a favorable safety profile[20,38].

Therefore, considering the difficulty in finding an effective treatment for this condition, medicinal cannabis represents an innovative and potentially useful alternative for managing oral mucositis[22,39,48,54].

Adverse Effects and Safety

In general, the reviewed articles report some common adverse effects associated with this therapy, including xerostomia (dry mouth), dizziness, and drowsiness[55]. Although phytocannabinoids, especially cannabidiol and Δ9-tetrahydrocannabinol, exhibit recognized therapeutic potential, their use may be associated with adverse effects and drug interactions that deserve attention, particularly in clinical contexts[47,55]. The most common side effects of THC include dry mouth (xerostomia), euphoria, dizziness, drowsiness, tachycardia, orthostatic hypotension, and at high doses, anxiety and cognitive alterations. CBD is generally better tolerated than THC but can cause drowsiness, appetite changes, fatigue, and mild gastrointestinal symptoms[56].

The dose administered in milligrams, dose titration, route of administration, and patient gender may also influence the appearance of adverse effects. Therefore, clinical monitoring and individualized treatment by qualified professionals are essential to adjust doses and avoid potential risks[52,57].

Drug Interactions

The use of medicinal cannabis can interact with other medications due to the way its compounds, such as cannabidiol (CBD) and tetrahydrocannabinol (THC), are metabolized in the body. These interactions occur mainly because of the influence of phytocannabinoids on enzymes of the CYP450 system, which metabolize many drugs. CYP refers to cytochrome P450, a superfamily of enzymes that play a crucial role in the metabolism of drugs and other xenobiotic substances in humans. Induction or inhibition of CYP enzymes is an important underlying mechanism of drug interactions. These enzymes are involved in oxidizing various substances, converting them into more watersoluble forms for elimination[58].

Both THC and CBD are metabolized by the hepatic cytochrome P450 enzymatic system, especially the isoenzymes CYP3A4 and CYP2C9 (in the case of THC) and CYP3A4 and CYP2C19 (for CBD). Thus, they may interfere with the metabolism of drugs using these same pathways, resulting in potentiated or reduced effects of concomitant medications, such as anticoagulants (warfarin), antiepileptics (clobazam, valproate), antidepressants, anxiolytics, and immunosuppressants[57].

The allopathic drugs that most frequently present interactions with cannabis include anticoagulants like warfarin, which may have their effects potentiated by cannabis use, increasing the risk of bleeding; antidepressants and anxiolytics, whose interaction with phytocannabinoids can intensify sedative effects or alter their efficacy; cannabis may also interfere with metabolism of antipsychotics, such as olanzapine, affecting their efficacy. The combination of opioids with phytocannabinoids can increase analgesic effects but also risks

of excessive sedation. Use of antiepileptics like clobazam along with these phytotherapeutics can alter plasma levels due to cannabis use, which may also lead to side effects. Alcohol consumption combined with cannabis can exacerbate THC effects, increasing risks of cognitive impairment and other side effects[57].

Therefore, it is essential to evaluate the patient's medical history before initiating phytocannabinoid therapy, especially in polypharmacy patients such as oncology patients or the elderly[56].

Regulation and Public Policies

The legal implications of cannabis use in Dentistry vary according to the legislation of each country. Currently in Brazil, the main regulations for prescription and medicinal cannabis include RDC nº. 660/2022[11], which defines importation as the means of acquiring cannabis-based products, including the prescription by the dental surgeon for granting import authorization, and RDC nº. 1015/2026[12], which although does not explicitly mention prescription by dental surgeons, Portaria nº. 344/1998[13] approves the technical regulation on substances and medications subject to special control, recognizing the dental surgeon as a prescriber of cannabis for medicinal purposes.

Some countries have already decided how to deal with medicinal cannabis. In the United States, for example, medicinal use is legalized in more than 30 states, although each state has its own regulations[14]. In Canada, both medicinal and recreational use have been fully legalized since 2018, and cultivation is also permitted for both personal and commercial use[15]. Germany legalized recreational use in 2024 and medicinal use is also legalized[16]. In the United Kingdom, recreational use is prohibited, but medicinal use is legalized; and in the Netherlands, consumption is decriminalized but sale is restricted to coffee shops[16]. These comparisons show that while some countries adopt a more liberal approach, others maintain more restrictive regulations. Brazil is at an intermediate stage, allowing medicinal use but with restrictions on recreational use and personal cultivation.

Conclusion

The results found in this literature review suggest that cannabis has promising therapeutic potential in Dentistry, with its main applications in the management oforofacial pain, periodontics, burning mouth syndrome, bruxism, management of oral mucositis, among others. Although mild adverse effects inherent to its use such as nausea and drowsiness are reported, it is considered a safe therapy. Challenges, however, include the need for more randomized clinical trials to standardize its use and assess long-term effects, thus providing a comprehensive view that will reinforce its use in clinical practice as well as in the creation of Public Policies and future research in the area.

Funding Sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Acknowledgements

The authors would like to express their gratitude to the School of Public Health of the Distrito Federal (ESPDF/FEPECS) and the State Secretariat of Health of the Distrito Federal (SES-DF) for their institutional support. The authors also would like to thank Paulo Henrique Silva Brandão Juhász for the technological support during the formatting of the article.

Contributions

Study conception: JAG, FVCP

Data curation: JAG, FVCP

Data collection: JAG, GAR, ESLC, DSC

Data analysis: JAG, FVCP

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Revision and editing: JAG, FVCP.

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Histórico do artigo | Submissão: 20/02/2026 | **Aceite:** 09/06/2026
Como citar este artigo: Grossi JÁ, Rodrigues GA, Capellini ESL, Coutinho DS, *et al*. Medicinal *Cannabis* in dentistry: a literature review. **Rev Fitos**. Rio de Janeiro. 2026; 20(1): e2011. e-ISSN 2446.4775. Disponível em: <https://doi.org/10.32712/2446-4775.2026.2011>. Acesso em: dd/mm/aaaa.