



The role of THC and CBD in dentistry – a review of impacts on oral health

Piotr Suski^{1,A-D}, Oskar Dominik Tokarczuk^{1,A-D}, Faustyna Nieroda^{1,B,D},
Karolina Thum-Tyzo^{2,D-F}

¹ Student Research Group at the Department of Oral Medicine, Medical University of Lublin, Lublin, Poland

² Department of Oral Medicine, Medical University of Lublin, Lublin, Poland

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Suski P, Tokarczuk OD, Nieroda F, Thum-Tyzo K. The Role of THC and CBD in Dentistry: A Review of Impacts on Oral Health. J Pre-Clin Clin Res. doi: 10.26444/jpccr/191337

Abstract

Introduction and Objective. The use of cannabinoids, particularly Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD), in dentistry has gained attention due to their therapeutic potential and complex pharmacokinetics. These cannabinoids interact with CB1 and CB2 receptors, which are crucial for managing pain, inflammation, and immune responses in oral health. This review examines the impact of cannabinoids on oral health, focusing on their therapeutic benefits and potential adverse effects in treating oral diseases.

Review Methods. The literature review utilized databases such as PubMed, ResearchGate, and Google Scholar, covering sources from 2003 – 2024. Key words included 'cannabinoids', 'oral health', 'THC', 'CBD', 'pharmacokinetics', 'marijuana adverse effects', 'periodontal disease', 'oral mucositis', 'dental pain management', and 'oral cancer'. Inclusion criteria focused on peer-reviewed articles, systematic reviews, clinical trials, case studies, and reviews involving human subjects or relevant animal models.

Brief description of the state of knowledge. Cannabinoids show promising therapeutic benefits, especially anti-inflammatory and analgesic effects, especially for treating chronic oral pain. However, adverse effects, such as increased risks of dental caries, periodontal disease, and potential oral cancers, have been noted, particularly with smoking. This complexity highlights the need for comprehensive studies to establish the efficacy and safety of cannabinoid use.

Summary. While cannabinoids hold potential for innovative dental treatments, their varying impacts due to different consumption methods and interactions with the oral microbiome necessitate further research. Future studies should focus on clarifying the clinical implications of cannabinoid use in dentistry for safe integration into healthcare.

Key words

endocannabinoid system, oral health, pharmacokinetics, Δ^9 -tetrahydrocannabinol (THC), Cannabinoids, cannabidiol (CBD), marijuana adverse effects

INTRODUCTION

Research into cannabinoids, particularly Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD), has grown significantly due to their extensive therapeutic potential and intricate pharmacokinetic profiles. THC is acknowledged as the main psychoactive ingredient in cannabis, while CBD is recognized for its non-psychoactive properties and its ability to moderate the psychoactive effects of THC. These cannabinoids function through the cannabinoid receptor type-1 (CB1) and cannabinoid receptor type-2 (CB2), which are crucial for managing a variety of physiological processes, including pain perception, inflammation, and immune responses [1]. The CB1 and CB2 receptors play a vital role in the endocannabinoid system, with CB1 mainly involved in neurotransmission, memory, and neuroprotection within the central nervous system. CB1 receptors are predominantly located in the brain and central nervous system, but are also found in peripheral tissues, including the gastrointestinal tract and reproductive

organs. CB2 receptors, on the other hand, are mainly found in peripheral tissues and immune cells, contributing to their role in modulating inflammation and immune function. Furthermore, cannabinoids interact with transient receptor potential vanilloid 1 (TRPV1) receptors, which are involved in pain and temperature regulation. The oral cavity also contains CB1 and CB2 receptors, which play roles in oral homeostasis and may contribute to the therapeutic potential of cannabinoids in treating conditions such as oral mucositis and pain [2].

Cannabinoids are divided into three groups: phytocannabinoids – naturally occurring in the *Cannabis sativa* plant (e.g. THC, CBD), endocannabinoids – produced within the human body (e.g. Arachidonylethanolamide, 2-arachidonoylglycerol), and synthetic cannabinoids – created to mimic the effects of natural cannabinoids (e.g. Dronabinol, Nabilone) [3].

The growing legalization of cannabis and the introduction of such new medical products as oils and edibles, considered safer than smoking, have fueled a rise in the use of medicinal *cannabis*. The variation in consumption methods significantly affects the bioavailability of cannabinoids, which differs based on the administration route. For instance, consuming *cannabis* orally typically leads to lower bioavailability of

✉ Address for correspondence: Oskar Dominik Tokarczuk, Student Research Group, Department of Oral Medicine, Medical University, Chodzki 6, 20-093 Lublin, Poland
E-mail: tokarczukoskar@gmail.com

Received: 13.06.2024; accepted: 14.07.2024; first published: 08.08.2024

THC due to first-pass liver metabolism, whereas inhalation provides quicker absorption and increased systemic availability [4]. The metabolism pattern of CBD is similar to the pattern of THC [1].

Historically, *Cannabis sativa* L. has been cultivated for its diverse uses, from food and fibre to medical applications. The plant is noted for containing over 100 cannabinoids that enhance its pharmacological activity. THC, originally present as Δ^9 -tetrahydrocannabinolic acid (THCA), must undergo decarboxylation, usually through a heating methods such as smoking or vaporization, to unlock its psychoactive properties [5].

Considering the profound effects of THC and CBD on the central nervous system, along with their potential anti-inflammatory and analgesic capabilities, it is crucial to understand how cannabis usage impacts oral health. Variations in cannabis strains and methods of consumption can produce different effects on oral tissues, potentially influencing conditions like gingivitis, periodontitis, and oral mucositis. Therefore, understanding the pharmacokinetics of THC and the dynamics of cannabinoid receptors is vital for addressing or preventing oral health issues [6].

OBJECTIVE

The primary aim of this review is to evaluate the impact of cannabinoid usage on oral health and its limitations due to adverse effects. The article database was sourced from PubMed, ResearchGate, and Google Scholar, with sources ranging from 2003 – 2024. Key words used for the search included ‘cannabinoids’, ‘oral health’, ‘ Δ^9 -tetrahydrocannabinol (THC)’, ‘cannabidiol (CBD)’, ‘marijuana adverse effects’, ‘endocannabinoid system’, ‘oral mucositis’, and ‘dental pain management’. The inclusion criteria focused on the oral health impact of cannabinoids in peer-reviewed journal articles, systematic reviews, meta-analyses, clinical trials, case studies, and reviews. A total of 741 articles were found. The selected articles were written in English and involved studies on human subjects or relevant animal models. In total, 26 articles were selected for inclusion in the review.

DISCUSSION

Medical implication of cannabinoids. Cannabinoids exhibit a range of effects on oral health, with therapeutic benefits and adverse outcomes. Studies indicate that THC is associated with negative effects, such as periodontal disease and oral cancer risk. In contrast, CBD shows promise due to its anti-inflammatory and analgesic properties, which may benefit conditions like chronic oral pain and inflammation [7,8]. Reviews highlight CBD’s potential in dental practices, including applications in periodontal therapy and bone regeneration, although the scarcity of clinical data calls for more rigorous studies to establish its efficacy and safety [9]. Moreover, broader research on medicinal cannabis suggests its utility in managing dental pain and enhancing healing, and emphasizes the need for regulatory and educational reforms for its integration into dental care [10]. Additionally, research conducted by Cretu et al. [11] on cannabinoids in oral cancer contexts suggests they may modulate tumour behaviour and potentially inhibit cancer cell proliferation.

The integration of cannabinoids into dentistry, therefore, presents both potential and challenges, necessitating further clinical trials and clearer regulatory guidelines.

Effects of cannabinoids on oral pain management. Recent studies on the impact of cannabinoids on managing dental pain have shown mixed results. The systematic review by Votrubec et al. [12] reveals limited evidence supporting the effectiveness of cannabinoids, with only one out of five studies noting significant benefits from a topical CBD formulation for temporomandibular disorder pain. A particularly noteworthy example is the study by Nitecka-Buchta et al. [13], which demonstrated that applying a transdermal CBD cream to the masseter muscles twice daily for 14 days significantly reduced pain intensity compared to a placebo. Chrepa et al. [14] report that CBD significantly alleviated acute dental pain, demonstrating effectiveness at various dosages and suggesting additional functional benefits, such as a improved bite force, which can positively affect decreasing mechanical allodynia. In the study, patients with moderate to severe toothache were given either 10 mg/kg or 20 mg/kg of CBD, or a placebo. Both CBD groups experienced significant reductions in pain compared to the placebo group, with the higher dose providing faster pain relief. Moreover, CBD treatment led to significant improvements in bite force, indicating enhanced dental function during the analgesic effect. Additionally, Laks et al. [15] provided pre-clinical evidence that β -caryophyllene, a non-psychoactive phytocannabinoid, effectively reduced pain and in rat pulp inflammation model, highlighting its potential as a non-opioid option for dental pain management. However, the review by Grossman et al. [6] indicates variability in the analgesic efficacy of cannabinoids, influenced by factors such as administration routes and specific cannabinoid compounds, with some clinical trials showing limited effectiveness. These findings emphasize the need for more comprehensive and well-designed clinical trials to better define the therapeutic role and safety of cannabinoids in treating orofacial pain. Lowe et al. [10] highlighted the potential of CBD in treating Burning Mouth Syndrome (BMS), a condition characterized by chronic burning sensations in the oral cavity. Studies identified the involvement of the endocannabinoid system (ECS) in BMS, with increased expression of the transient receptor potential vanilloid 1 (TRPV1) and CB2 receptors and decreased CB1 receptor expression in the epithelial cells of the tongue. Clinical trials demonstrated the safety and efficacy of cannabinoids, including CBD, in alleviating BMS symptoms, suggesting that targeting the ECS could be an effective therapeutic strategy.

Impact of cannabinoids on salivary glands and salivation. The impact of cannabinoids on salivation has been a significant focus due to the common symptom of dry mouth associated with various conditions and treatments, including *cannabis* use. Research indicates that cannabinoids interact with salivary secretion pathways primarily via cannabinoid receptors. Prestifilippo et al. [16] found that cannabinoids inhibit salivation through activation of both CB1 and CB2 receptors in the submandibular glands of rats, affecting receptor-mediated signalling that usually promotes fluid secretion. Similarly, Andreis et al. [17] observed in the animal model that THC and similar compounds might reduce salivation by influencing the neuronal control of

salivary glands, particularly through CB1 receptors on the axons of cholinergic neurons. They reported that THC, at a dose of 4 mg/kg administered intraperitoneally (IP), significantly reduced salivation in both male and female mice. Similarly, the CB1 receptor agonist CP55940, at a dose of 0.5 mg/kg (IP), also lowered saliva volume. It was also noted that the modulation of endocannabinoid metabolism by fatty acid amide hydrolase (FAAH) is a significant factor, as inhibition or deletion of FAAH led to reduced salivation. Furthermore, cannabidiol (CBD), at a dose of 4 mg/kg (IP), did not affect salivation on its own, but was able to reverse the effects of THC in a concentration-dependent manner. Busch et al. [18] further explored this topic by demonstrating that anandamide activates CB1 receptors in the rat parotid gland, leading to changes such as increased cyclic adenosine monophosphate (cAMP) accumulation and inhibited Na⁺-K⁺-ATPase activity, which are crucial for gland function, and could potentially be harnessed therapeutically to treat salivary gland disorders. The studies on animals cited above collectively highlight how cannabinoid-induced modulation might be applied in therapeutic contexts of salivary secretion dysfunction and gland diseases.

Cannabinoids in oral mucosa diseases. The potential therapeutic applications of cannabinoids in periodontology garner interest, particularly due to their immunomodulatory and antibacterial properties. Studies suggest that fibroblasts incubated with CBD at concentrations ranging from 0.01 – 30 μM effectively manage periodontal diseases by modulating inflammation and oxidative stress within gingival tissues, thereby protecting against periodontal degradation. [19,20]. Additionally, its antioxidant properties may alleviate oral mucositis, a condition common in chemotherapy and radiotherapy patients [21]. Meanwhile, THC has been shown to facilitate periodontal healing and tissue regeneration by enhancing cellular adhesion and migration via the CB2 receptor and focal adhesion kinase (FAK) signalling pathway [22].

Although the results are promising, the wider impact of cannabinoid use, especially smoking, suggests a possible link to worsening periodontal health, akin to the effects of tobacco. This creates a contradictory situation in periodontal treatment [23]. Furthermore, studies like those of Apostu et al. [24] and Carmona Rendón et al. [25] suggest that cannabinoids could significantly influence bone metabolism and periodontal tissue homeostasis through their action on cannabinoid receptors in osteoblasts and osteoclasts, potentially opening new avenues for periodontal treatments. Studies have demonstrated that specific doses of cannabinoids, such as 10 nM to 300 nM, can effectively stimulate osteoblast activity and inhibit osteoclast function, highlighting their therapeutic potential in maintaining bone and periodontal health. This dichotomy underscores the need for a nuanced understanding of the effects of cannabinoids on periodontal tissues to balance therapeutic benefits against potential adverse impacts.

Lowe et al. [10] indicated that CBD might be beneficial in treating oral mucositis, a condition often resulting from cancer-related chemotherapy and radiation, characterized by inflammation and ulceration of the mucous membranes. Although the evidence is not extensive, CBD's antioxidant properties suggest it may help manage oxidative stress linked to oral mucositis. CBD's ability to modulate cannabinoid

receptors and exert anti-inflammatory effects points to a potential new therapeutic approach for this condition.

CBD has also been effective in managing recurrent aphthous ulcers (RAU). In a randomized controlled trial, Umpreecha et al. [26] found that applying 0.1% CBD oral paste to RAUs three times daily for seven days significantly reduced ulcer size and erythematous borders compared to placebo, especially in early treatment stages. CBD also demonstrated notable analgesic effects, reducing pain scores more effectively by day five, with higher patient satisfaction and no adverse reactions observed.

Qi X et al. [27] demonstrated significant therapeutic potential of CBD in managing oral ulcers (OU). Topical application of CBD on acid- or trauma-induced OUs in mice tongues, with doses of 1 mg/mL and 10 mg/mL, resulted in reduced inflammation, pain relief, and accelerated healing. Notably, the higher dose (10 mg/mL) was associated with better therapeutic effects. This effectiveness is attributed to the ability of CBD to inhibit the NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome pathway, and decrease inflammatory cytokines like Interleukin-1 beta (IL-1β) and Interleukin-18 (IL-18). Histological analysis showed reduced inflammation and increased proliferation in the subepithelial layer of CBD-treated ulcers, indicating enhanced healing. CBD also suppressed cytidine monophosphate kinase 2 (CMPK2) expression, reducing mitochondrial DNA synthesis and further inflammasome activation. Overall, CBD facilitated mucosal barrier restoration and provided significant analgesic effects, making it a promising therapeutic option for managing OUs.

Adverse effects of cannabinoids. Despite the recognized therapeutic benefits of cannabinoids such as THC and CBD, their adverse effects on oral health merit significant attention. Studies have consistently linked cannabis consumption, especially through smoking, with detrimental oral health outcomes including xerostomia, increased dental caries, periodontal disease, and even oral cancers [28]. These negative outcomes are attributed to the immunosuppressive and carcinogenic properties of cannabis smoke, which directly exposes oral tissues to harmful compounds.

Further research by Newman et al. [29] confirms that chronic marijuana smoking alters the oral microbiome, heightening the risk of oral infections and potentially malignant disorders, e.g. oral leukoplakia and erythroplakia, which may progress to oral squamous cell carcinoma (OSCC) under sustained exposure. These findings are particularly concerning as shifts in the oral microbial flora linked to chronic cannabis use could predispose individuals to both periodontal disease and carcinogenesis. Moreover, while non-psychoactive cannabinoids like CBD are celebrated for their anti-inflammatory properties, although their impact on the oral microbiome and overall oral health remains poorly understood. Preliminary studies suggest that CBD could influence cellular mechanisms and enzymatic pathways within the oral cavity, possibly disrupting normal cellular activities and promoting dysbiosis [30].

Although the systematic review by Ghasemiesfe et al. [31] indicates a low-strength link between marijuana use and certain types of cancer, including oral cancers, the evidence remains inconclusive due to study limitations such as minimal exposure levels and brief follow-up durations. Additionally, the research highlighted by Huestis et al. [32]

discusses the potential carcinogenic effects of cannabinoids like THC, underscoring the complex relationship between their therapeutic and harmful potentials, and emphasizing the need for more comprehensive research to fully understand the long-term impacts of cannabinoid exposure on oral health.

It is important to emphasize the problem of psychosis, induced by cannabis use with a dose-response effect observed in the study of Beckmann et al [33]. Daily use and high potency THC (the psychoactive compound in cannabis) carry the highest risk. THC potency in cannabis has risen significantly. It has been proven that daily users of high potency cannabis had over four times the risk of developing a psychotic disorder compared to non-users. Switching to lower THC cannabis halved the risk, even with continued daily use. This study provided the first direct evidence that cannabis use increases the incidence of psychotic disorders, suggesting that the high potency cannabis can trigger the onset of first-episode psychosis in some individuals [33].

CONCLUSIONS

In summary, recent studies on the cannabinoids THC and CBD highlight their intricate impact on oral health, blending positive therapeutic effects with possible negative outcomes. THC is linked to adverse health issues such as periodontal diseases and oral cancers, largely because of its immunosuppressive qualities. On the other hand, CBD shows significant promise due to its anti-inflammatory and pain-relieving properties, which may help alleviate chronic oral conditions. The complex effects of cannabinoids call for a detailed understanding of their pharmacokinetics and their interaction with the endocannabinoid system in oral tissues. The variability in how cannabinoids are administered and the different strains used also add layers of complexity to their effects on oral health, underscoring the necessity for rigorous clinical trials and robust regulatory measures to manage their use in oral medicine.

It must not be forgotten that despite the many positive aspects of cannabinoids, those consumed through smoking, particularly marijuana containing THC, carry very negative mental and physical adverse effects, such as periodontal diseases, the formation of leukoplakia and erythroplakia, which can increase the risk of developing cancer, especially OSCC. With the increasing legalization of cannabis and the introduction of new cannabinoid-based products, there is a pressing need for comprehensive research to ensure a safe balance between their benefits and risks, facilitating their responsible incorporation into oral disease treatment and wider medical applications.

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