



NARRATIVE REVIEW

Cannabinology in Dentistry: Therapeutic Applications and Future Directions

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Abstract

Cannabinology, the study of compounds derived from *Cannabis sativa* and their interactions with the endocannabinoid system (ECS), has gained increasing relevance in dentistry. Cannabinoids such as cannabidiol (CBD) and tetrahydrocannabinol (THC) demonstrate therapeutic potential in the management of orofacial pain, dental anxiety, periodontal inflammation, and tissue regeneration [1,2]. This narrative review explores the biological basis of cannabinoid action in oral tissues, clinical applications, regulatory challenges, and future perspectives for cannabinoid-based therapies in dental practice [3]. Despite promising preliminary evidence, more robust clinical trials are needed to establish safety, efficacy, and standardized therapeutic protocols [4]. The integration of cannabinology into dental education and research can expand the therapeutic arsenal available to oral health professionals.

Keywords

Cannabinology, Dentistry, Cannabidiol, Orofacial pain, Periodontal inflammation, Tissue regeneration

Introduction

Cannabinology, the field that studies compounds derived from *Cannabis sativa* and their effects on the organism, has gained prominence in dentistry

[5]. Cannabinoids such as CBD and THC interact with the endocannabinoid system (ECS), which regulates essential functions such as pain, inflammation, and immune response [1,6]. Dental interest grows due to therapeutic potential in conditions such as orofacial pain, anxiety, periodontal inflammation, and tissue regeneration [7]. With advancing research and progressive legislative flexibility in various countries, cannabinoids are being considered promising therapeutic options, especially for chronic conditions refractory to conventional treatments [3].

The Endocannabinoid System and its Relevance in Dentistry

The ECS is composed of cannabinoid receptors (CB1 and CB2), endocannabinoids (endogenous agonists such as anandamide and 2-AG), and synthesis and degradation enzymes [1,8]. The CB1 receptor is abundantly expressed in the central nervous system, while CB2 is found predominantly in immune system cells. Both receptors are expressed in multiple oral cavity tissues, including tongue, salivary glands, dental pulp, periodontal tissues, and oral mucosa [6,9]. Activation of these receptors modulates crucial physiological processes such as inflammatory response, nociception,

and tissue healing, which provides the foundation for their vast therapeutic potential in dentistry [10,11].

Clinical Applications of Cannabinoids in Dentistry

Orofacial pain and Temporomandibular dysfunction (TMD)

TMD represents one of the main causes of orofacial pain of non-dental origin [12]. CBD, due to its capacity to modulate CB1 and CB2 receptors and suppress the release of inflammatory cytokines, demonstrates significant potential in relieving joint and muscle pain associated with TMD [3,13]. Preclinical studies indicate that phytocannabinoids and terpenes exert robust antinociceptive effects in neuropathic and inflammatory pain models [14].

Dental anxiety

CBD exhibits notable anxiolytic effects, primarily through modulation of the hypothalamic-pituitary-adrenal (HPA) axis and interaction with the serotonergic system [15]. Preclinical studies demonstrate that CBD is capable of reducing conditioned fear and anxiety-associated behaviors, suggesting a potential benefit for managing patients with dental anxiety and phobia [16,17].

Periodontal diseases

Although recreational cannabis use in smoked form is associated with increased periodontal risk, isolated cannabinoids, such as CBD, exhibit potent anti-inflammatory and antimicrobial properties [18,19]. CB1 and CB2 receptors play a role in regulating cellular differentiation and periodontal ligament healing [20]. The expression of these receptors is altered in inflammatory conditions, positioning them as promising therapeutic targets [21].

Tissue regeneration

Emerging evidence suggests that CBD may favor osteogenic and odontoblastic differentiation, promoting reparative dentin formation and dentino-pulpal complex regeneration [22]. Human dental pulp stem cells (hDPSCs) treated with CBD demonstrate greater mineralization capacity and exhibit immunomodulatory properties in inflammatory environments, highlighting their potential for dental tissue engineering [23].

Other potential applications

- Xerostomia: CB receptors are involved in modulating salivary secretion, opening pathways for dry mouth treatment [11].
- Nausea and Vomiting: Cannabinoids are clinically used for controlling chemotherapy-induced nausea and vomiting in oncology patients [24].
- Oral Mucositis: CBD has demonstrated efficacy in reducing severe oral inflammation induced by chemotherapy in preclinical models [25].

Scientific Evidence and Limitations

Review of studies and knowledge gaps

Most evidence regarding cannabinoid use in dentistry is still based on preclinical studies (in vitro and animal) [4]. The scarcity of randomized controlled clinical trials in humans represents a significant barrier for defining therapeutic protocols, dosage regimens, and ideal administration routes [3,26]. The heterogeneity of cannabis chemovars and available extracts also complicates standardization and result reproducibility.

Potential adverse effects

Cannabinoid use is not without risks. Adverse effects may include xerostomia, dizziness, and somnolence. Regarding oral health, cannabis smoking is associated with increased risk of periodontal diseases [18]. Systemic impacts such as tachycardia, cognitive alterations, and immunosuppression should also be considered, as well as risks associated with use during pregnancy, such as low birth weight [27,28].

Regulatory and Ethical Aspects

International regulatory landscape

The legal status of cannabinoids for medicinal purposes varies substantially between countries. Nations such as Canada, Germany, Australia, and several U.S. states have established regulatory frameworks that allow prescription by healthcare professionals. Pharmacovigilance initiatives, such as the Quebec Cannabis Registry in Canada, are fundamental for monitoring clinical use and adverse effects on a large scale, generating real-world data that are essential to complement clinical trial evidence [29,30,31].

Ethical challenges and professional training

There is a notorious gap in cannabinology training in dental undergraduate curricula worldwide [4,5]. It is imperative that dentists be trained to discuss risks and benefits, obtain informed consent, and responsibly integrate cannabinoid use into the patient's medical history.

Future Perspectives

Dental-specific formulations

The future of cannabinology in dentistry lies in developing topical and local application formulations, such as gels, orodispersible films, oral rinses, and biomaterials (cements, scaffolds), aimed at maximizing local therapeutic effect with minimal systemic absorption and effects [8,12].

Curricular integration

The formal inclusion of endocannabinoid system pharmacology in undergraduate and graduate dental curricula is fundamental for preparing the next generation of professionals to prescribe these therapies safely, effectively, and evidence-based [4,5].

Future research and interdisciplinary collaboration

The research agenda should prioritize: robust clinical trials on orofacial pain, TMD, and periodontal diseases; studies to elucidate molecular mechanisms of action in oral tissues; long-term safety and efficacy evaluation; and the development of controlled-release systems specific to the oral cavity [3,4,32].

Conclusion

Cannabinology presents a promising frontier in dentistry, offering innovative approaches for managing chronic pain, anxiety, inflammation, and tissue regeneration. Despite enormous potential, translation to routine clinical practice requires overcoming regulatory, ethical, and scientific challenges. Adequate professional training, promotion of high-quality clinical research, and interdisciplinary collaboration will be decisive for consolidating the therapeutic and safe use of cannabinoids as a valuable tool in the oral health arsenal.

Key Contributions of this work

- Comprehensive review of cannabinoid applications in dentistry
- Analysis of the endocannabinoid system's role in oral health
- Discussion of regulatory and ethical considerations
- Identification of future research priorities

Conflict of Interest

None declared.

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References

1. Casadoumeq AC, Fernández-Solari JJ, Elverdin JC, Rodríguez PA, Mohn CE (2023) The role of the endocannabinoid system in tooth eruption: An ex vivo study. *Aust Endod J* 49: 79-88.
2. Abidi AH, Alghamdi SS, Derefinko K (2022) A critical review of cannabis in medicine and dentistry: A look back and the path forward. *Clin Exp Dent Res* 8: 613-631.
3. Grossman S, Tan H, Gadiwalla Y (2022) Cannabis and orofacial pain: A systematic review. *Br J Oral Maxillofac Surg* 60: e677-e690.
4. Carmona-Rendón Y, Garzón HS, Bueno-Silva B, Arce RM, Suárez LJ (2023) Cannabinoids in periodontology: Where are we now? *Antibiotics* 12: 1687.
5. Fernandes G, de Almeida S, Nagarkatti P, et al. (2023) Cannabinoids in Dentistry: Where are we now? *Int J Oral Dent Health* 9:134.
6. Votrubec C, Tran P, Lei A, Brunet Z, Bean L, et al. (2022) Cannabinoid therapeutics in orofacial pain management: A systematic review. *Aust Dent J* 67: 314-327.
7. Pires-Lohr RB, Leles CR, Arantes DAC, Morais MO, Freitas NMA, et al. (2024) Potential applications of cannabinoids in dentistry and oncology-short communication. *Oral Surg Oral Med Oral Pathol Oral Radiol* 137: e301-e302.
8. Campana MD, Paolis G, Sammartino G, Bucci P, Aliberti A, et al. (2025) Cannabinoids: therapeutic perspectives for management of orofacial pain, oral inflammation and bone healing-A systematic review. *Int J Mol Sci* 26: 3766.
9. Di Marzo V, Bifulco M, De Petrocellis L (2004) The endocannabinoid system and its therapeutic exploitation. *Nat Rev Drug Discov* 3: 771-784.
10. Heilicz S, Wilensky A, Gaver T, Georgiev O, Hamad S, et al. (2022) Salivary endocannabinoid profiles in chronic orofacial pain and headache disorders: An observational study using a novel tool for diagnosis and management. *Int J Mol Sci* 23: 13017.
11. Habib G, Steinberg D, Jabbour A (2021) The impact of medical cannabis consumption on the oral flora and saliva. *PLoS One* 16: e0247044.
12. Mulla SA, Patil A, Mali S, Jain AK, Jaiswal H, et al. (2024) Unleashing the therapeutic role of cannabidiol in dentistry. *J Oral Biol Craniofac Res* 14: 649-654.
13. Velly AM, Anderson GC, Look JO, Riley JL, Rindal DB, et al. (2022) Management of painful temporomandibular disorders: Methods and overview of The National Dental Practice-Based Research Network prospective cohort study. *J Am Dent Assoc* 153: 144-157.
14. Wanasuntronwong A, Kaewsrisung S, Rotpenpian N, Arayapisit T, Pavasant P, et al. (2022) Efficacy and mechanism of the antinociceptive effects of cannabidiol on acute orofacial nociception induced by Complete Freund's Adjuvant in male *Mus musculus* mice. *Arch Oral Biol* 144: 105570.
15. Mazzantini C, El Bourji Z, Parisio C, Davolio PL, Cocchi A, et al. (2024) Anti-inflammatory properties of cannabidiol and beta-caryophyllene alone or combined in an in vitro inflammation model. *Pharmaceutics* 17: 467.
16. García-Gutiérrez MS, Navarrete F, Gasparyan A, Austrich-Olivares A, Sala F, et al. (2020) Cannabidiol: A potential new alternative for the treatment of anxiety, depression, and psychotic disorders. *Biomolecules* 10: 1575.
17. Luján MÁ, Alegre-Zurano L, Martín-Sánchez A, Valverde O (2020) The effects of cannabidiol on cue- and stress-induced reinstatement of cocaine seeking behavior in mice are reverted by the CB1 receptor antagonist AM4113. *BioRxiv*.
18. Chaffee BW (2021) Cannabis use and oral health in a national cohort of adults. *J Calif Dent Assoc* 49: 493-501.
19. Chen H, Liu Y, Yu S, Li C, Gao B, et al. (2023) Cannabidiol attenuates periodontal inflammation through inhibiting TLR4/NF-κB pathway. *J Periodontal Res* 58: 697-707.
20. Monteiro Viana JC, Silva Gomes GE, Duarte Oliveira FJ, Marques de Araújo LN, Teles G, et al. (2024) The role of different types of cannabinoids in periodontal disease: an integrative review. *Pharmaceutics* 16: 893.
21. Zamith Cunha R, Zannoni A, Salamanca G, De Silva M, Rinnovati R, et al. (2023) Expression of cannabinoid (CB1 and CB2) and cannabinoid-related receptors (TRPV1, GPR55, and PPARα) in the synovial membrane of the horse metacarpophalangeal joint. *Front Vet Sci* 10: 1045030.
22. Li L, Feng J, Sun L, Xuan YW, Wen L, et al. (2022) Cannabidiol promotes osteogenic differentiation of bone marrow mesenchymal stem cells in the inflammatory microenvironment via the CB2-dependent p38 MAPK signaling pathway. *Int J Stem Cells* 15: 405-414.

23. Sales LS, Silva-Sousa AC, Nascimento GC, Del Bel E, Paula-Silva FWG (2025) Effects of cannabidiol on biomineralization and inflammatory mediators expression in immortalized murine dental pulp cells and macrophages under pro-inflammatory conditions. *J Dent* 153: 105535.
24. Bathula PP, Maciver MB (2023) Cannabinoids in treating chemotherapy-induced nausea and vomiting, cancer-associated pain, and tumor growth. *Int J Mol Sci* 25: 74.
25. Moniruzzaman M, Janjua TI, Martin JH, Begun J, Popat A (2024) Cannabidiol - Help and hype in targeting mucosal diseases. *J Control Release* 365: 530-543.
26. Bellocchio L, Inchingolo AD, Inchingolo AM, Lorusso F, Malcangi G, et al. (2021) Cannabinoids drugs and oral health-from recreational side-effects to medicinal purposes: A systematic review. *Int J Mol Sci* 22: 8329.
27. Renard J, Konefal S (2022) Clearing the smoke on cannabis: Cannabis use during pregnancy and breastfeeding - an update. Canadian Centre on Substance Use and Addiction, Ottawa.
28. Crippa JA, Pereira LC, Zimmermann PM, Brum L, Rechia LM, et al. (2021) Effect of two oral formulations of cannabidiol on responses to emotional stimuli in healthy human volunteers: pharmaceutical vehicle matters. *Braz J Psychiatry* 44: 15-20.
29. Sheikh NK, Dua A (2023) Cannabinoids. StatPearls Publishing, Treasure Island, FL.
30. Crippa JAS, Hallak JEC, Machado-de-Sousa JP, Queiroz RHC, Bergamaschi M, et al. (2013) Cannabidiol for the treatment of cannabis withdrawal syndrome: A case report. *J Clin Pharm Ther* 38: 162-164.
31. Onaivi ES, Sharma V (2020) Cannabis or marijuana: what is in a name? *J Altern Complement Med* 26: 1006-1014.
32. Russo EB (2011) Taming THC: Potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol* 163: 1344-1364.