

Editorial



Cannabinoids in periodontal disease amid the COVID-19 pandemic

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OPEN ACCESS

Received: Nov 24, 2020

Accepted: Dec 2, 2020

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Cannabis sativa contains more than 140 terpene-like compounds, called cannabinoids, that share the cannabinoid chemical scaffold. The 2 main members of this chemical family are Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD) [1]. Animal and human studies have demonstrated that THC is responsible for the majority of the intoxicating effects of cannabis; it acts by binding to G protein-coupled cannabinoid (CB) receptors in the brain and other tissues of the body. By contrast, CBD exhibits a distinct set of pharmacological properties, including anti-epileptic and anti-inflammatory effects that are mostly independent of CB receptor activation [1,2].

It is notable that the use of cannabis is associated with a higher prevalence of periodontitis (for a systematic review, see [3]). Data obtained from the National Health and Nutrition Examination Survey (NHANES) indicate that frequent use of recreational cannabis is positively associated with severe periodontitis, which was observed both in a bivariate analysis and in a multivariable analysis adjusted for demographics (age, sex, race/ethnicity, and income level), alcohol and tobacco use, diabetes mellitus, and past periodontal treatment [4]. Research has also found that cannabis may produce adverse effects on oral tissues including gingival enlargement, nicotinic stomatitis, and uvulitis [5].

Remarkably, a number of beneficial effects have also been reported. Considerable evidence supports that pharmacological strengthening of the endogenous cannabinoid (endocannabinoid) system may exert beneficial effects on periodontal inflammation and nerve pain [6]. CBD was shown to exert anti-inflammatory and anti-oxidative effects resulting in a faster resolution of oral mucositis in a murine model [7]. Additionally, enhancing endocannabinoid signaling in cells that initiate local immune responses in the periodontium, the periodontal ligament cells, significantly dampened their pro-inflammatory responses to lipopolysaccharide (LPS) produced by *Porphyromonas gingivalis* [8]. It has been also shown that selective agonists for type 2 CB (CB₂) receptors exert anti-inflammatory effects in human periodontal ligament fibroblasts [9]. Finally, pharmacological activation of the endocannabinoid system in periodontal ligament cells exhibited host-protective effects by both dampening inflammation and preserving cellular integrity, while palmitoylethanolamide, a bioactive lipid structurally related to endocannabinoids, exacerbated inflammation [10]. All in all, these results suggest that targeting the endocannabinoid system, in particular by boosting local CB₂ receptor signaling, may lead to novel therapeutics that improve current treatments for periodontal disease and other oral inflammatory pathologies [11].

The coronavirus disease 2019 (COVID-19) pandemic due to the worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has significantly affected the use of cannabis in 2 particular human populations, among others. First, it was shown that those who engaged in self-isolation used 20% more cannabis during the pandemic than those who did not, which was associated with self-reported isolation and loneliness [12]. In addition, people with mental health conditions reported increased use of medicinal cannabis by 91% during the COVID-19 pandemic, compared to those with no mental health conditions [13]. Therefore, during the pandemic, health care providers should pay particular attention to oral diseases. Importantly, communication and cooperation between physicians and dental practitioners should be encouraged in managing and treating patients. In addition, the seemingly opposite contribution of the 2 main ingredients of cannabis, THC and CBD, to periodontitis should be kept in mind when addressing the effects of cannabinoids. Certainly, further research is required to evaluate the beneficial and harmful effects of various phytocannabinoids and pharmacological modulators of the endocannabinoid system.

REFERENCES

1. Jung KM, Piomelli D. Cannabinoids and endocannabinoids. In: Pfaff DW, Volkow ND, editors. Neuroscience in the 21st century: from basic to clinical. New York (NY): Springer New York; 2016. p.1811-41.
2. Cristino L, Bisogno T, Di Marzo V. Cannabinoids and the expanded endocannabinoid system in neurological disorders. *Nat Rev Neurol* 2020;16:9-29.
[PUBMED](#) | [CROSSREF](#)
3. Chisini LA, Cademartori MG, Francia A, Mederos M, Grazioli G, Conde MC, et al. Is the use of Cannabis associated with periodontitis? A systematic review and meta-analysis. *J Periodontal Res* 2019;54:311-7.
[PUBMED](#) | [CROSSREF](#)
4. Shariff JA, Ahluwalia KP, Papapanou PN. Relationship between frequent recreational cannabis (marijuana and hashish) use and periodontitis in adults in the United States: National Health and Nutrition Examination Survey 2011 to 2012. *J Periodontol* 2017;88:273-80.
[PUBMED](#) | [CROSSREF](#)
5. Rawal SY, Tatakis DN, Tipton DA. Periodontal and oral manifestations of marijuana use. *J Tenn Dent Assoc* 2012;92:26-31.
[PUBMED](#)
6. Xiong W, Cui T, Cheng K, Yang F, Chen SR, Willenbring D, et al. Cannabinoids suppress inflammatory and neuropathic pain by targeting $\alpha 3$ glycine receptors. *J Exp Med* 2012;209:1121-34.
[PUBMED](#) | [CROSSREF](#)
7. Cuba LF, Salum FG, Guimarães FS, Cherubini K, Borghetti RL, de Figueiredo MA. Cannabidiol on 5-FU-induced oral mucositis in mice. *Oral Dis* 2020;26:1483-93.
[PUBMED](#) | [CROSSREF](#)
8. Zhang F, Özdemir B, Nguyen PQ, Andrukhov O, Rausch-Fan X. Methanandamide diminish the *Porphyromonas gingivalis* lipopolysaccharide induced response in human periodontal ligament cells. *BMC Oral Health* 2020;20:107.
[PUBMED](#) | [CROSSREF](#)
9. Abidi AH, Presley CS, Dabbous M, Tipton DA, Mustafa SM, Moore BM 2nd. Anti-inflammatory activity of cannabinoid receptor 2 ligands in primary hPDL fibroblasts. *Arch Oral Biol* 2018;87:79-85.
[PUBMED](#) | [CROSSREF](#)
10. Jäger A, Setiawan M, Beins E, Schmidt-Wolf I, Konermann A. Analogous modulation of inflammatory responses by the endocannabinoid system in periodontal ligament cells and microglia. *Head Face Med* 2020;16:26.
[PUBMED](#) | [CROSSREF](#)
11. Abidi AH, Alghamdi SS, Dabbous MK, Tipton DA, Mustafa SM, Moore BM. Cannabinoid type-2 receptor agonist, inverse agonist, and anandamide regulation of inflammatory responses in IL-1 β stimulated primary human periodontal ligament fibroblasts. *J Periodontal Res* 2020;55:762-83.
[PUBMED](#) | [CROSSREF](#)

12. Bartel SJ, Sherry SB, Stewart SH. Self-isolation: a significant contributor to cannabis use during the COVID-19 pandemic. *Subst Abus.* Forthcoming 2020.
[PUBMED](#) | [CROSSREF](#)
13. Vidot DC, Islam JY, Marlene Camacho-Rivera , Harrell MB, Rao DR, Chavez JV, et al. The COVID-19 cannabis health study: results from an epidemiologic assessment of adults who use cannabis for medicinal reasons in the United States. *J Addict Dis.* Forthcoming 2020.
[PUBMED](#) | [CROSSREF](#)