Minireview Article

Cannabidiol, the journey of Cannabis from a social stigma to a miracle drug in Dentistry.

Abstract

In recent years, there has been a surge in the awareness regarding the phyto cannabinoid; cannabidiol. Between the time period from 1963 to 2000, only 460 publications can be found in a PubMed search while using cannabidiol as the keyword. The former pales in comparison to the record of 2769 publications found from 2008 to the present time. However, a limited amount of literature is available that discusses the therapeutic potential of cannabidiol, pertaining to the field of dentistry. In 1940, cannabidiol was isolated from cannabis for the first time, its structure being reported much later in 1963. Further research on Cannabis resulted in the declaration that "THC" is the active compound. Subsequent studies were then directed essentially based on the virtual exclusion of cannabidiol and other cannabinoids from cannabis. This was primarily due to the belief that the activity of cannabis was merely psychological activity.

In retrospect, this seems unfortunate as many of the beneficial properties of cannabidiol which might have had a therapeutic benefit were overlooked. In the present review, attention will be focused on the therapeutic potential of Cannabidiol and the impact this may have on dentistry with the supplemental vision of encouraging further studies to reveal any other beneficial properties that may be present.

Keywords- Cannabinoid, Dentistry, Analgesia, Antibacterial, Osteogenesis, Myorelaxant

Introduction

When the topic of cannabis comes into discussion, the first thing that comes to mind are its psychoactive properties and tendency for drug abuse. However, evidence of the usage of cannabis sativa or marijuana has been appreciated in ancient medicine. There are a various number of traditional medical sciences which utilise it for its numerous properties. The only physical evidence of its use in ancient medical practice was be dated back to 400 AD. (1). Through extensive research in the field, it was ascertained that it is THC (Δ^{9}-tetrahydrocannabinol) which causes a psychotomimetic effect or "the high". Cannabidiol on its own is not capable of producing such an effect. Rather CBD boasts of a wide range of medicinal properties which might prove to be therapeutic. Some of these properties include but may not be limited to an antipsychotic effect (2,3) , analgesic property, neuroprotective effect, antiemetic effect, antioxidation, anti-epileptic, anti-inflammatory (4,5) , anti-arthritic, and anti-neoplastic properties. These are being researched to be uncover the true therapeutic potential of cannabidiol. They may also be a useful aid in the general dental practice in various situations that are further described.

Procedure- We carried out a review of the literature on the subject in the PubMed database. We used the keywords 'cannabinoids', 'cannabidiol', and 'Dentistry' to search for full articles published in English from 1963 to 2021. Additional papers were obtained from the reference lists in the 'hits'.

Classic and more recent studies covered Controlling Inflammation, Oral prophylactic potential, Treating Anxiety, Analgesic & Post-Treatment Pain Management, Osteogenic potential and The Future of Cannabidiol in Dentistry.

Controlling Inflammation

Many clinical and in vitro studies have assessed the anti-inflammatory effects of CBD and came up with promising results (4) (5) (6) (7). Artificially induced oral ulcers as demonstrated in the experimental procedure in Wistar rats presented with a significantly lower inflammatory score (8). In another study conducted on mice, researchers induced oral mucositis in CF-1 strain mice using 5-fluororacil chemotherapy alternatively known as 5-FU chemotherapy. On evaluating the clinical outcome, it was observed that the groups treated with cannabidiol exhibited a lowered intensity of the lesion when compared with the positive control group (9).Hence, it was inferred that CBD might display anti-inflammatory properties which can be useful as medication after oral surgical procedures such as dental implants, exodontia, etc. The iatrogenic inflammation induced by periodontal procedures such as scaling and root planning may also be reduced with the use of CBD.

Oral prophylactic potential

Bactericidal properties of CBD have also been demonstrated by researchers in a study where they collected dental plaque from participants to observe the effect of cannabinoids on bacterial reduction against other commercially available toothpastes (Colgate, Oral-b, Cannabite F). They found that all the groups in which cannabinoids were administered, presented with a lower bacterial count than commercially available toothpastes. They included all possible stages of periodontal status ranging from non-bleeding gums to gums having increased resorption of bone and increased mobility of teeth. (10). This implies that it might play a role in averting infections of the oral cavity.

Treating dental Anxiety

Anxiety and fear are adapted responses which through evolution are essential to cope with any threat which might endanger survival of the organism. Similar psychological and physiological responses are observed all over the world in the patients undergoing dental treatment. These responses serve only to further scare the patient and hinder the clinician with regards to dental procedures. (11). Simply ignoring this issue may lead to phobia, degraded interest towards care seeking for oral health and even discontinuing the ongoing treatment. (12) (13). For patients and doctors seeking a way to substitute the routinely used medications for relief from dental anxiety, CBD presents a great choice. CBD has been researched extensively for the purpose of relief from various anxiety related disorders. It could potentially help in reducing feelings of discomfort and preventing episodes of panic on the dental chair. The fact that Cannabidiol has proven itself an effective anxiolytic drug in animal model studies, led the way to research in human subjects. It was not before 1980s when clinical research was attempted to examine effects of Cannabidiol on anxiety. Interestingly cannabidiol was found to cause attenuation of anxiety and psych activity that was caused by THC in the healthy subjects (2). Subsequent studies took a step forward wherein they involved healthy subjects and individuals that were diagnosed with social anxiety disorder to make it evident that cannabidiol may be capable of resolving anxiety in humans (3) (14) (15). In a study on patients with severe anxiety disorder such as post-traumatic stress disorder it was revealed that administration of Cannabidiol orally along with routine psychiatric care may result in reduction of symptoms (7). To affirm this fact, modification of blood flow in specific structures of brain (cingulate cortex, amygdala, hippocampus and hypothalamus) that are associated with

anxiety are seen on neuroimaging techniques post cannabidiol administration (15) (16). With the aid of Cannabidiol, clinicians can avoid the conventional sedation techniques such as nitrous oxide and Benzodiazepines along with their side effects thereby achieving an improved safety profile. This helps in obtaining relief from their anxiety and discomfort whilst undergoing dental procedures.

Analgesic & Post-Treatment Pain Management

Our knowledge of the function of cannabidiol in pain management has yet to broaden; evidently the analgesic effect of cannabidiol is seen due to modulation & interaction of numerous involved systems (inflammatory, nociceptive and endocannabinoid systems) (17). Health Canada has already approved its use for pain management in multiple sclerosis in 2005. In 2007, they approved cannabidiol as a therapeutic drug in cancer pain that is unresponsive to conventional opioid therapy (18). Cannabidiol has also shown great potential in management of pain in subjects diagnosed with myofascial pain (19). It has also proven itself to be a strong analgesic when used to treat other difficult-to-manage pain. This implies that cannabidiol may be a potential alternative to conventionally used pharmaceuticals when it comes to the treatment and management of pain experienced oral carcinoma, burning mouth syndrome, salivary gland stones, neuralgia and after an oral surgery like a tooth extraction or implant placement. While traditional pharmaceuticals like opiates are effective at controlling pain, they are highly habit-forming and often cause uncomfortable side effects like hyperacidity, nausea & vomiting (20). Cannabidiol offers a suitable alternative which is a more natural technique of managing pain free of side effects.

Osteogenic potential

A group of researchers conducted a study to evaluate effects of cannabidiol on differentiation mesenchymal stem cells and compare them with vitamin D3. Mesenchymal stem cells derived from apical papilla; dental follicle & dental pulp were utilised for the experiment. The study concluded that even a minute dose of cannabidiol can enhance the cell differentiation drastically, particularly for the dental follicle and apical papilla (21). Another study was conducted on rat models, wherein artificially induced periodontal lesion were treated with cannabidiol mixed in a saline vehicle.

Myorelaxant effect

Most of the intraoral dental procedures force the patient to open their mouth for long periods of time to enable better illumination and visualisation of the working field by the clinician. If procedure is time consuming it can cause muscle fatigue thereby decreasing the mouth opening which in turn will reduce the visibility and accessibility of the clinician leading to an increase in the chair time. Increased durations of mouth opening may also precipitate the development of Temporomandibular disorders or might aggravate the pre-existing conditions already present in the patient which would regrettably be iatrogenic and be easily avoidable with the use of appropriate medications, for which cannabidiol is a candidate (19).

The Future of Cannabidiol in Dentistry

A greater number of studies needs be conducted so that a proper dosing protocol along with appropriate, prescribed and controlled usage of cannabidiol in the general dental scenario can be established. There are many benefits associated with cannabidiol and it may yet prove to be useful for both, clinicians and patients when it comes to the management of pain, inflammation, and anxiety in the clinical set-up. Owing to its all-natural composition coupled with the absence of any major complications, it would not be startling to see an increase in the utilization of cannabidiol in dental offices and become a norm in the not-so-distant future.

Conclusion

Cannabidiol is novel and fast emerging pharmacological alternative to many conventional drugs in dentistry. As described in many alternative medicine practices, with more research and innovative approach, it could become miraculous one for all drug in dentistry as well.

References

1. *Early medical use of cannabis. Nature.* Zias J, Stark H, Sellgman J, et al. Early medical use of cannabis. Nature. 1993.

3. *Cannabidiol interferes with the effects of delta 9-tetrahydrocannabinol in man. Eur J Pharmacol.* Karniol IG, Shirakawa I, Kasinski N, et al.

4. *Cannabidiol, extracted from Cannabis sativa, selectively inhibits inflammatory hypermotility in mice.* Capasso, Raffaele, et al. 5, 2008, British Journal of Pharmacology, Vol. 154, pp. 1001-1008.

5. *Anti-inflammatory role of cannabidiol and O-1602 in cerulein-induced acute pancreatitis in mice.* Li, Kun, et al. 1, 2013, Pancreas, Vol. 42, pp. 123-129.

6. *The effects of Δ9-tetrahydrocannabinol and cannabidiol alone and in combination on damage, inflammation and in vitro motility disturbances in rat colitis.* Jamontt, Joanna, et al. 3, 2010, British Journal of Pharmacology, Vol. 160, pp. 712-723.

7. *Analgesic and antiinflammatory activity of constituents of Cannabis sativa L.* Formukong, E. A., Evans, A.T. and Evans, Fred J. 4, 1988, Inflammation, Vol. 12, pp. 361-371.

8. *Effects of cannabidiol, a Cannabis sativa constituent, on oral wound healing process in rats: Clinical and histological evaluation.*

9. *Cannabidiol on 5-FU-induced oral mucositis in mice.* Letícia de Freitas Cuba, PhDa, et al. Porto Alegr : s.n., May 13, 2020.

10. *Comparison of Efficacy of Cannabinoids versus Commercial Oral Care Products in Reducing Bacterial Content from Dental Plaque: A Preliminary Observation.*

11. *Characteristics of adult dentally fearful individuals. A cross-cultural study.* U Berggren, C J Pierce, I Eli.

12. *Oral health-related quality of life in patients with dental anxiety.* Mats Mehrstedt, Mike T John, Sven Tönnies, Wolfgang Micheelis.

14. *Effects of ipsapirone and cannabidiol on human experimental anxiety. J Psychopharmacol.* Zuardi AW, Cosme RA, Graeff FG, et al.

15. *Effects of Cannabidiol (CBD) on Regional Cerebral Blood Flow.* José Alexandre de Souza Crippa, Antonio Waldo Zuardi, Griselda E J Garrido, Lauro Wichert-Ana, Ricardo Guarnieri, Lucas Ferrari, Paulo M Azevedo-Marques, Jaime Eduardo Cecílio Hallak, Philip K McGuire & Geraldo Filho Busatto.

16. *Distinct Effects of Δ9-Tetrahydrocannabinol and Cannabidiol on Neural Activation During Emotional Processing.* Fusar-Poli P, Crippa JA, Bhattacharyya S, et al.

17. *Pharmacological actions and therapeutic uses of cannabis and cannabinoids.* R N Kumar, W A Chambers, R G Pertwee.

18. *Cannabinoids in the management of difficult to treat pain.* Russo, Ethan B.

19. *Myorelaxant Effect of Transdermal Cannabidiol Application in Patients with TMD: A Randomized, Double-Blind Trial.* Aleksandra Nitecka-Buchta, OrcID, Anna Nowak-Wachol, Kacper Wachol, Karolina Walczyńska-Dragon, Paweł Olczyk OrcID, Olgierd Batoryna OrcID, Wojciech Kempa and Stefan Baron. 2019.

20. *CBD: A natural remedy for dental anxiety.* CHEBBI, DR. YASMIN.

21. *Cannabidiol and Vitamin D3 Impact on Osteogenic Differentition of human dental mesenchymal stem cells.* al, Nausica B. Petrescu et.

22. *Safety and side effects of cannabidiol, a Cannabis sativa constituent.* Bergamaschi, Mateus M., et al. 4, 2011, Current Drug Safety, Vol. 6, pp. 237-249.

23. *Effects of cannabidiol, a Cannabis sativa constituent, on oral wound healing process in rats: Clinical and histological evaluation.* Figueiredo, Mariana Klein Juliane de Quadros De Bortolli Francisco Silveira Guimarães Fernanda Gonçalves Salum Karen Cherubini Maria Antonia Zancanaro de. 08 August 2018.

24. *Action of cannabidiol on the anxiety and other effects produced by delta 9-THC in normal subjects. Psychopharmacology (Berl).* Zuardi AW, Shirakawa I, Finkelfarb E, et al.