Scholastic Medical Science

Review article

Volume 2 Issue 3 - 2024

Therapeutic Indications of Cannabis Sativa in Odontology for Autistic Patients: A Literature Review

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Received: April 25, 2024**; Published:** May 08, 2024

Abstract

Objective: The aim of this study is to investigate and critically analyze the potential therapeutic applications and effects of Cannabis sativa, particularly focusing on its cannabinoids, in the field of dentistry.

Methodology: To conduct this research, a comprehensive literature review was undertaken. This involved querying several databases for relevant scientific articles and studies. Key databases included BVS/BIREME, PubMed Central, Web of Science, ScienceDirect, the Periodic Portal from CAPES, The Cochrane Library, and PROSPERO.

Results: The endocannabinoid system, along with various cannabinoids, plays a multifaceted role in immune regulation and inflammation. These components show potential in therapeutic applications, ranging from modulating immune cell function to treating inflammatory diseases.

Keywords: Cannabis, Cannabinoids, Dentistry.

Introduction

Autism Spectrum Disorder (ASD) can be described as a neurodevelopmental disorder that encompasses a wide spectrum varying in severity and stereotyped symptoms. These symptoms include deficits in communication, difficulty in comprehending signs and linguistic variations, social interaction challenges, restricted interests characterized by hyperfocus, and repetitive behaviors. Anxiety conditions are also prevalent, along with bursts of anger and the need for a future life projection (7).

Cannabis sativa, commonly known as marijuana, has sparked controversy in recent years due to its criminal stigma, often accompanied by legislative issues. However, despite these challenges, its medical efficacy has increasingly gained recognition, especially in treating patients with special conditions, including autism(24). In this context, this review explores and analyzes the scientific literature concerning the use of Cannabis sativa in dentistry, particularly highlighting its effects on anxiety, pain intensity, inflammatory situations, and other aspects relevant to dental practice.

Recent findings suggesting that Cannabis sativa may play a role in reducing periodontal inflammation have spurred the construction of this article, offering innovative approaches and possibilities for managing periodontal disease(1), which is a significant concern for autistic patients. This plant, rich in phytochemical cannabinoid compounds, presents a wide range of therapeutic alternatives to address such innovative issues within the scientific community. The effects of cannabinoids on the Central Nervous System (CNS) are mediated by the plant's receptors distributed throughout most of its cells, as well as in peripheral tissues. The current literature is substantial enough to support a direct impact of Cannabis sativa on physiological activities essential to dental clinical practice.

In order to explore new modalities of dental care with the already studied mechanisms of action of cannabinoids, it is natural for dental practitioners to investigate them for patients in need of extra care and attention, such as the autistic community(9). Whether used alone or in conjunction with allopathic medication, Cannabis sativa has become a valuable tool for the available dental therapeutic arsenal, contributing to evidence-driven debates in this promising field.

Materials and methods

To accomplish this paper, a meticulous literature review was conducted. Therefore, several databases were consulted for relevant scientific articles and studies. The primary ones included BVS/BIREME, PubMed Central, Web of Science, ScienceDirect, the Periodic Portal from CAPES, The Cochrane Library, PROSPERO, as well as Google Scholar. The objective of this paper was to explore the scientific literature regarding the application of Cannabis sativa in dental practice for autistic patients, with particular emphasis on facilitating treatment procedures through the use of cannabis.

Literature Review

Autism Spectrum Disorder (ASD)

The characteristics of individuals with autism may vary significantly from one person to another, ranging from slight signs which many times go undetected, to more severe situations, such as those autistic patients who hurt or mutilate themselves due to excess of brain electric stimulations. It is regarded as a neurological disorder characterized by impaired social interaction, verbal and non-verbal communication, and restricted and repetitive behavior (15). Signs usually develop gradually, but some autistic children reach the developmental milestone at a normal rate and, all of a sudden, regress.

The main manifested sign is usually not staring at people (22). Some common characteristics include: Communication difficulties: some individuals with autism may struggle to understand and use verbal language appropriately. This can include challenges in understanding figurative language, expressing emotions, and interpreting tone of voice and body language. Repetitive behaviors: People with autism often exhibit repetitive behavior patterns, such as body rocking, hand flapping, or repeating words or phrases, sometimes for hours(17). Such behaviors may be the only way they use of coping with stress or anxiety.

Autistic patients also develop specific and intense non-stopping interests. Many of them have hyperfocus on certain themes or areas of knowledge; and depending on the degree of the spectrum, they may be extremely productive for artistic, medical and many other fields of human labor(3). They may deeply dedicate themselves to these specific interests and have detailed and scrutinized knowledge about them, regardless of how old they are. Some individuals with autism may even have heightened sensory sensitivities, meaning they are more sensitive to stimuli such as bright lights, loud noises, textures, or strong odors; others may show synesthetic features, which usually cause discomfort or anxiety in specific environments, such as crowded or colorful places.

Many autistic individuals with autism struggle to understand and participate in social interactions in typical ways. This might include difficulties in making friends, interpreting social cues, or understanding the nuances of interpersonal relationships. It is important to note that while these characteristics are common in individuals with autism, each person is unique and may exhibit a different combination of symptoms and traits. Additionally, autism is a fundamental part of a person's identity, and many individuals with autism have valuable skills and talents that can be appreciated and celebrated, since many celebrities have along the trajectory of their career proclaimed themselves as autistics.

Risperidone in Autism Spectrum Disorder

Risperidone, commercially known as Risperdal, is an atypical antipsychotic medication that has garnered approval for the treatment of irritability associated with autism spectrum disorders in children and adolescents. This pharmaceutical is also utilized for addressing schizophrenia and bipolar disorder in adults. The therapeutic benefits of risperidone in autism primarily stem from its ability to mitigate symptoms such as aggression, temper tantrums, and self-harm.

The efficacy of risperidone is linked to its pharmacological properties, where it functions as an antagonist at both dopamine D2 receptors and serotonin 5-HT2A receptors. By inhibiting these neurotransmitter receptors, risperidone facilitates the modulation of mood and the stabilization of erratic behaviors that are often exacerbated by excessive neurotransmitter activity. Additionally, risperidone's interaction with alpha-1 adrenergic and histamine H1 receptors contributes to its side effect profile, notably sedation and potential orthostatic hypotension(10).

Pharmacokinetically, risperidone is characterized by good oral absorption, achieving peak plasma concentrations one to two hours post-administration, with an approximate bioavailability of 70%. The liver metabolizes it into its active metabolite, 9-hydroxyrisperidone, also known as paliperidone, which plays a significant role in the medication's therapeutic effects. The elimination half-life of risperidone and its metabolite varies among individuals, which necessitates personalized adjustments in dosing intervals(2).

Clinically, risperidone has demonstrated substantial efficacy in alleviating behavioral disturbances associated with autism, generally manifesting improvements within four to six weeks of initiation. Despite its effectiveness, risperidone is associated with several side effects. Common adverse effects include weight gain, sedation, and gastrointestinal disturbances, while more severe risks involve metabolic syndrome, extrapyramidal symptoms, and elevated prolactin levels(12). These potential adverse effects underscore the necessity for meticulous monitoring. Regular evaluations of weight, metabolic health, and neurological status are imperative, with therapeutic adjustments made in response to these assessments and the patient's overall treatment response.

In conclusion, while risperidone presents a vital pharmacological option for managing certain symptoms of autism spectrum disorders, its administration demands a comprehensive treatment strategy encompassing behavioral therapies and other supportive interventions. Such an integrated approach ensures a holistic response to the diverse needs of individuals afflicted with autism, optimizing outcomes while vigilantly managing the risk of adverse effects.

Cannabis Hemp

Hemp seed oil, derived from the seeds of *Cannabis sativa L.*, is distinguished by its high content of essential fatty acids, making it highly beneficial for nutritional use. It contains about 55% linoleic acid (omega-6) and 20% alpha-linolenic acid (omega-3), with a favorable omega-6 to omega-3 ratio of approximately 3:1, which is considered ideal for human health(20). This oil also includes smaller amounts of gamma-linolenic acid and stearidonic acids, enhancing its health-promoting profile.

The formulation of stable oil-in-water emulsions using hemp seed oil with non-ionic surfactants such as Tween and Span. It was found that high-energy emulsification methods were particularly effective, producing emulsions with smaller particle sizes, around 151 ± 1 nm(13). The concentration and type of surfactants played crucial roles in determining the stability and size of the emulsion particles. However, despite these advancements in emulsion technology, the anticipated

increase in antibacterial activity of the emulsions was not observed. While hemp seed oil demonstrated modest antibacterial properties against bacteria like Micrococcus luteus and Staphylococcus aureus, these properties were not significantly enhanced in the emulsified form(27).

This combination of nutritional richness and the potential for functional food applications makes hemp seed oil a valuable ingredient in the food industry. Its essential fatty acid content can contribute to heart health and cholesterol management, marking it as a significant component for dietary enhancement(5). Although the study revealed limited antibacterial enhancement in emulsified forms, hemp seed oil remains a promising candidate for health-oriented food products.

Furthermore, the unique properties of hemp seed oil, particularly its ideal fatty acid composition, are being explored for their role in supporting mental health. Omega-3 fatty acids are crucial for brain health, and their anti-inflammatory properties may benefit individuals suffering from mood disorders such as depression and anxiety[6]. As research progresses, hemp seed oil could potentially become a key component in nutraceuticals aimed at cognitive and emotional well-being, leveraging its bioactive compounds to contribute to a holistic approach to health. This broader application of hemp seed oil underscores its versatility and the growing interest in plant-based compounds in various sectors of health and wellness.

Results

Table 1: State of art for Cannabis Sativa

Period	Use and study	Observations
Antiquity	Medicinal use in civilizations like the Chinese and Hindus; ritual and role recreational.	References in the Vedas of India and writings of Herodotus in ancient Greece.
19th Century	Gained attention in Western medicine; commercially available cannabis-based products.	Used to treat neuralgia, insomnia, and menstrual pain.
Early 20th Century	Decline in medicinal use; increased stigmatization.	Influenced by the enactment of substance control laws.
Second half of the 20th Century	Resurgence of scientific interest; discovery of the endocannabinoid system.	Expanded research, strict prohibition policies.

Table 2: Chemical Characteristics of Cannabis Sativa

Component	Prescription	Potential Effects
Cannabinoids (THC, CBD)	Interact with cannabinoid receptors in the nervous system.	THC: psychoactive effects. CBD: therapeutic benefits without psychoactivity.
Terpenes	Responsible for the characteristic aroma.	-
Flavonoids	Have antioxidant properties.	-
"Entourage Effect"	Complex interaction between chemical components.	Importance in the diversity of effects on the human body.

Table 3: Regulation of Inflammation in Dentistry

Treatment	Purpose	Importance
Scaling and root planing, antimicrobial therapies	Reduction of inflammation in periodontal diseases.	Critical for the prevention and treatment of gingivitis and periodontitis.
Post-surgical management	Reduction of inflammation and promotion of healing.	Essential after tooth extractions and dental implant placements.
Anti-inflammatory medications	Dental pain management.	Common in pain management practices.
Decay prevention	Application of dental sealants and fluoride treatments.	Reduces the risk of inflammation and related dental issues.

Table 4: Management of autistic patients

Condition	CBD Efficacy	Notes
Autism and other neurological disorders	Therapeutic potential in various disorders.	Interacts with multiple targets within the CNS.
Epilepsy	Antiepileptic.	-
Chronic pain	Analgesic.	-
Neurodegenerative diseases (e.g., Alzheimer's)	Neuroprotective.	-

Discussions

Throughout history, Cannabis Sativa has been utilized across diverse cultural landscapes, notably within Chinese and Hindu medicinal traditions, thus underscoring its enduring therapeutic significance. Its assimilation into Western medicine during the 19th century for ailments such as neuralgia, insomnia, and menstrual pain marked a broader acknowledgment of its medicinal properties(28). However, the 20th century bore witness to a significant paradigm shift with escalating stigmatization and prohibition, followed by a resurgence in scientific interest, particularly subsequent to the revelation of the endocannabinoid system. This transition underscores the evolving perception of cannabis, shaped by cultural, legal, and scientific determinants.

The intricate chemical composition of the plant is highlighted by its constituents, including cannabinoids (such as THC and CBD), terpenes, and flavonoids. THC is renowned for its psychoactive effects, whereas CBD is esteemed for its non-psychoactive therapeutic potential. The notion of the 'entourage effect', delineating the synergistic interaction of these compounds, suggests diverse therapeutic applications in dentistry, implying that distinct compositions of cannabis might yield varied effects.

Inflammation plays a central role in periodontal diseases and postoperative healing. Conventional treatments have hitherto relied upon mechanical procedures and anti-inflammatory medications. The potential of Cannabis Sativa as an anti-inflammatory agent presents an innovative alternative, conceivably beneficial in managing periodontal diseases, post-surgical healing, and inflammation due to orthodontic tooth movement.

Endocannabinoids, alongside their metabolic enzymes and receptors, assume a pivotal role in the immune system, being ubiquitous in cells such as monocytes, macrophages, and lymphocytes. These molecules function in an autocrine and paracrine capacity, modulating immune responses to uphold homeostasis. Notably, CB1 receptors are predominantly expressed on B cells, NK cells, and T cells, accentuating the extensive involvement of the endocannabinoid system in immune function(11).

Particularly, the CB2 receptor emerges as indispensable in immune cell dynamics. For instance, human B cells evince an increase in CB2 expression post-activation, albeit a decrease during their differentiation process[19]. In macrophages, CB2 expression levels fluctuate contingent upon the activation state of the cell and the presence of inflammation. This dynamic expression of CB2 receptors significantly impacts immune cell functions, particularly in inflammatory conditions, thus suggesting a pivotal role of the endocannabinoid system in immune regulation.

Moreover, two pivotal endocannabinoids, 2-arachidonoylglycerol (2-AG) and anandamide (AEA), merit recognition for their immunomodulatory roles, chiefly through their interaction with CB2 receptors. These molecules partake in critical immune regulatory processes, encompassing the inhibition of pro-inflammatory cytokines and the modulation of intracellular signaling pathways, thereby underscoring the significance of these endocannabinoids in maintaining immune homeostasis and their potential therapeutic applications.

An intriguing facet of the endocannabinoid system lies in its interaction with Toll-like receptors (TLRs). This interaction entails cannabinoids modulating the inflammatory responses induced by TLRs, thereby hinting at a complex interplay between the endocannabinoid system and innate immunity.

As elucidated in the investigation by(16), in the intricate orchestration of the body's response to inflammation, particularly within the central nervous system (CNS), cannabinoids such as cannabidiol (CBD) assume a nuanced and pivotal role. Just as the body's innate defenses orchestrate acute inflammatory reactions through the action of macrophages and the secretion of pro-inflammatory cytokines, cannabinoids function in a parallel yet distinct pathway to modulate these responses. CBD, in particular, exerts its influence by engaging with a constellation of receptors, including TRPV1, CB2, and GPR55, each playing a pivotal role in the modulation of inflammation.

This receptor interaction represents merely the initial stage. The downstream effects of these engagements are profound: there's a marked downregulation of key enzymes, such as inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX2), which are integral in the production of inflammatory mediators like prostaglandins, reactive oxygen species, and cytokines such as tumor necrosis factor-alpha (TNF-α). CBD's influence extends further to the molecular signaling cascades, where it inhibits the MAPK (mitogen-activated protein kinases) pathways and downregulates NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells), a pivotal player in the inflammatory process.

Beyond these pathways, CBD also activates PPARγ (peroxisome proliferator-activated receptor gamma), which plays a role in reducing lipid peroxidation, a process often upregulated in inflammatory states(18). This action of CBD mirrors the body's natural inflammatory response, where mast cells release vasoactive amines and arachidonic acid metabolites, leading to the clustering and migration of neutrophils towards the inflamed tissue(8).

Just as the body's response to inflammation entails a delicate balance of pro-inflammatory and anti-inflammatory forces, with mechanisms such as the secretion of C-reactive protein and C3 complement protein synthesized by the liver in response to TNF-α, IL-1β, IL-6, IL-12, and chemokines signaling, CBD's interaction with the body's endocannabinoid system offers a nuanced counterbalance. It establishes a form of negative feedback, akin to the intricate interplay between the neuroendocrine axis and the immune system, thereby spotlighting the complexity and finesse of the body's response to injury and infection(25).

By potentially mitigating inflammation and promoting healing, CBD might proffer a more comfortable and efficient recovery for patients

undergoing dental surgeries or treatments that typically culminate in postoperative inflammation and pain(14). Additionally, its anxiolytic effects could prove advantageous for patients grappling with dental anxiety, a common impediment to seeking requisite dental care. The utilization of CBD in dental practices might not only ameliorate patient outcomes in terms of healing and comfort but also potentially curtail reliance on traditional pain medications, which often entail side effects and risks of dependency(21). As research continues to burgeon, the integration of CBD into dental treatments could herald a significant shift towards more holistic and patient-centered care in dentistry, addressing both physiological and psychological facets of oral health and treatment experiences(26).

The review posits that Cannabis Sativa could efficaciously manage dental pain and anxiety, recurrent challenges in dental practice(23). Its plausible utilization in treating gum diseases and regulating postoperative inflammation and pain could revolutionize certain aspects of dental care. Nevertheless, this realm confronts challenges, including disparate global legal status and the imperative for rigorous clinical trials to delineate its efficacy, safety, and usage guidelines in dentistry.

Conclusions

The endocannabinoid system, along with various cannabinoids, plays a nuanced role in immune regulation and inflammation. These elements exhibit potential in therapeutic applications, spanning from modulating immune cell function to treating inflammatory diseases. As research in this area continues to evolve, the understanding and utilization of cannabinoids in medical science will likely expand, offering new avenues for the treatment and management of various conditions.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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