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Ariane Caroline Castro Alves[1], Roberto Gama de Oliveira[2], Julia de Araújo Koplowitz Bento[3], Diego Barbosa da Silva[4], Jennifer Vera Santos Gumert[5], Guilherme Alchaar Sodré Duarte[6], Adnaleila Silva de Medeiros Brandão[7], Giselle Amiska Soares[8], Cecilia de Oliveira Costa Amorim[9], Flavio Eduardo Brandão[10], Tatiana Klein Alvaracci[11], Larissa Ferreira Lourenço Auad[12], Beatriz Rezende de Oliveira[13], Rhayara Pires Ferreira de Assunção[14], Eduardo Francisco de Souza Faco[15], Octávio Olivio Fuzzo[16], José da Silva Júnior[17], Tereza Regina Péres Vaz[18], Marco Antonio Teixeira Candido[19]

ABSTRACT

Guided bone regeneration (GBR) is a widely used technique in implant dentistry to restore bone quantity and quality in areas with defects, aiming at implant success. In recent years, cannabidiol (CBD), a phytocannabinoid from Cannabis sativa, has shown promising therapeutic properties in regenerative processes due to its modulatory effects on inflammation, osteogenesis, and bone remodeling. This article presents a literature review of experimental and clinical studies on the effects of CBD on bone regeneration, analyzing its mechanisms of action, safety, efficacy, and potential applications in implant dentistry. Findings

[1] Dentist Surgeon, Implantologist. Faculdade Unicastelo. E-mail: odontocastroalves@gmail.com
[2] Master in DTM/DOF. São Leopoldo Mandic. E-mail: roberto.oliv2010@hotmail.com
[3] Dental Student. Universidade Federal Fluminense (UFF). E-mail: juliaakoplowitz@gmail.com
[4] Dentist Surgeon. Universidade Maurício de Nassau. E-mail: diegobarbosa234@gmail.com
[5] Periodontology Specialist. Centro Universitário UniDomBosco. E-mail: jennifergumert@yahoo.com
[6] Dentistry Student. E-mail: guilhermealchaar@gmail.com
[7] Dentistry Student. Centro Universitário Maurício de Nassau (UNINASSAU). E-mail: adnaleila@yahoo.com.br
[8] Dental Student. Centro de pós-graduação em Odontologia. E-mail: giselleamiska@hotmail.com
[9] Dentist Surgeon. CTBMF Specialist. Associação Brasileira de Odontologia.
E-mail: cecicostaamorim@gmail.com
[10] Dentist Surgeon. Specialist in Implantology. Centro Universitário Vale do Rio Verde (UninCor).
E-mail: feduardobrandao@yahoo.com.br
[11] Biomedical. Centro Universitário em Itu e Salto SP (Ceunsp). E-mail: Tatiana_kdm@yahoo.com.br
[12] Dentistry Student. Centro Universitário UNA. E-mail: larissa.lourencoferreiras@gmail.com
[13] Dentist Surgeon. Dental Prosthesis Specialist. Universidade de Santo Amaro (Unisa).
E-mail: dra.beatrizoliveira@gmail.com
[14] Dentistry Student. Universidade de Rio Verde (UniRV). E-mail: rhay.assuncao@gmail.com
[15] Doctor of Implantology. Universidade Estadual Paulista (UNESP). E-mail: efsfaco@gmail.com
[16] Dentistry Student. Universidade de São Caetano do Sul (USCS).
E-mail: octaviofuzzo@gmail.com
[17] Doctor of Dental Sciences (Implantology). São Leopoldo Mandic. Instituto RC de Pós-graduação.
E-mail: jrsilvacmk79@gmail.com
[18] Master. E-mail: tperes.vaz@gmail.com
[19] Master's student in Biotechnology. Universidade de Gurupi (UNIRG) | UFT | Especializações em Ortodontia, DTM/DOF e Saúde Pública. E-mail: m.antonio1991@hotmail.com

indicate that CBD promotes osteoblast differentiation, inhibits osteoclast activity, reduces inflammation, and enhances graft integration, creating a favorable environment for healing and implant success. Although results are promising, controlled clinical studies are needed to establish standardized therapeutic protocols and define safe doses. The incorporation of CBD in GBR represents an innovative perspective for personalized regenerative treatments, contributing to significant advances in modern implant dentistry.

Keywords: Cannabidiol. Guided Bone Regeneration. Implant Dentistry. Osteogenesis. Biomaterials.

RESUMO

A regeneração óssea guiada (ROG) é uma técnica amplamente utilizada na implantodontia para restaurar a quantidade e a qualidade óssea em áreas que apresentam déficits, visando o sucesso dos implantes dentários. Nos últimos anos, o canabidiol (CBD), um fitocanabinoide da Cannabis sativa, tem demonstrado propriedades terapêuticas promissoras em processos regenerativos, devido à sua ação moduladora sobre a inflamação, osteogênese e remodelação óssea. Este artigo realizou uma revisão bibliográfica de estudos experimentais e clínicos relacionados ao efeito do CBD na regeneração óssea, analisando seus mecanismos de ação, segurança, eficácia e potenciais aplicações na implantodontia. Os achados indicam que o CBD promove a diferenciação de osteoblastos, inibe a atividade de osteoclastos, reduz a inflamação e favorece a integração de enxertos ósseos, oferecendo um ambiente favorável para a cicatrização e o sucesso de implantes. Embora os resultados sejam promissores, há necessidade de estudos clínicos controlados para estabelecer protocolos terapêuticos padronizados e definir doses seguras. A incorporação do CBD na ROG representa uma perspectiva inovadora para tratamentos regenerativos personalizados, contribuindo para avanços significativos na implantodontia moderna.

Palavras-chave: Canabidiol. Regeneração Óssea Guiada. Implantodontia. Osteogênese. Biomateriais.

RESUMEN

La regeneración ósea guiada (ROG) es una técnica ampliamente utilizada en implantología dental para restaurar la cantidad y calidad ósea en zonas deficientes, con el objetivo de garantizar el éxito de los implantes dentales. En los últimos años, el cannabidiol (CBD), un fitocannabinoide de Cannabis sativa, ha demostrado prometedoras propiedades terapéuticas en procesos regenerativos gracias a su acción moduladora de la inflamación, la osteogénesis y la remodelación ósea. Este artículo realizó una revisión bibliográfica de estudios experimentales y clínicos relacionados con el efecto del CBD en la regeneración ósea, analizando sus mecanismos de acción, seguridad, eficacia y posibles aplicaciones en implantología dental. Los hallazgos indican que el CBD promueve la diferenciación de osteoblastos, inhibe la actividad de los osteoclastos, reduce la inflamación y favorece la integración del injerto óseo, proporcionando un entorno favorable para la cicatrización y el éxito del implante. Si bien los resultados son prometedores, se necesitan estudios clínicos controlados para establecer protocolos terapéuticos estandarizados y definir dosis seguras. La incorporación del CBD a la ROG representa una perspectiva innovadora para los tratamientos regenerativos personalizados, contribuyendo a avances significativos en la implantología dental moderna.

Palabras clave: Cannabidiol. Regeneración Ósea Guiada. Implantología. Osteogénesis. Biomateriales.

1 INTRODUCTION

Guided bone regeneration (GBR) has established itself as one of the main approaches in dentistry and implant dentistry for the treatment of areas with significant bone loss, being decisive for the success of dental implants in compromised regions (JIRÁSEK et al., 2022). The technique is based on the use of physical barriers, usually biocompatible membranes, which allow the selective migration of osteogenic cells and prevent the invasion of soft tissues, favoring the formation of new bone tissue.

In recent years, the literature has been dedicated to the search for strategies that enhance ROG, either by developing new biomaterials or by incorporating bioactive substances capable of modulating regenerative processes. Among these agents, cannabidiol (CBD), a non-psychoactive phytocannabinoid derived from *Cannabis sativa*, has aroused great interest due to its anti-inflammatory, analgesic, and osteoinductive properties (KOTURBASH; MACKAY, 2020; KLEIN et al., 2018).

Experimental evidence suggests that CBD exerts a positive influence on osteogenesis through multiple cellular and molecular mechanisms. Studies indicate that the compound favors the osteogenic differentiation of mesenchymal stem cells and dental pulp cells, regulating signaling pathways such as JNK, p38 MAPK and Wnt/β-catenin, which are fundamental for osteoblastic maturation and bone matrix deposition (LIU et al., 2019; GU et al., 2019). In addition, CBD modulates the expression of osteogenic transcription factors, such as Runx2 and Osterix, which are central elements for the formation of mature osteoblasts and for the mineralization of bone tissue (CARMONA RENDÓN et al., 2023). This osteoinductive effect is especially relevant in situations of alveolar bone loss and in patients with limited regenerative capacity, such as the elderly and individuals with chronic inflammatory diseases.

Another aspect of note is the anti-inflammatory and immunomodulatory action of CBD, considered essential for the success of ROG. The exacerbated inflammatory response at surgical sites can compromise bone regeneration and increase the risk of implant failure, making it necessary to balance initial inflammation and subsequent repair (ABIDI et al., 2020). In this context, CBD acts by regulating the release of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, reducing the excessive inflammatory process and establishing a microenvironment conducive to osteogenic proliferation and differentiation (KONERMANN et al., 2017). Also noteworthy is the activation of the cannabinoid receptor CB2, associated with protection against alveolar bone loss in periodontitis models, evidencing the importance of

the endocannabinoid system in bone homeostasis and in the control of local inflammatory processes (KOZONO et al., 2010).

Additionally, CBD influences key steps in bone healing, such as migration, adhesion, and cell proliferation. In *vitro* assays demonstrate that the compound stimulates the migration of osteoprogenitor cells to the site of injury, accelerating bone filling in critical defects (BERNARDINI et al., 2018). Also noteworthy is its ability to induce the synthesis of extracellular matrix, especially type I collagen and matrix proteins, which confers greater structural stability to the regenerated tissue and improves bone density. These effects position CBD as a promising adjuvant in biomaterials, bone grafts, controlled-release systems, and topical formulations applied directly to regeneration areas (JIRÁSEK et al., 2022).

In the clinical setting, incorporating CBD into ROG may offer benefits that transcend osteogenesis. Its analgesic and anti-inflammatory action contributes to the reduction of postoperative pain and edema, improving the patient experience and favoring adherence to therapeutic protocols. Preclinical evidence indicates that animals treated with CBD have lower local inflammation and higher bone density compared to controls, suggesting that the combined application to ROG membranes can accelerate healing and increase the clinical predictability of dental implants (KLEIN et al., 2018; GU et al., 2019).

However, despite the promising results, the clinical application of CBD still faces limitations. The definition of the ideal dose, the most appropriate route of administration, and the duration of application remains open, requiring randomized clinical trials to validate its efficacy. In addition, long-term safety should be carefully investigated, considering potential pharmacological interactions and individual response variability (KONERMANN et al., 2017; CARMONA RENDÓN et al., 2023). Pharmacokinetic issues, such as low oral bioavailability and extensive hepatic metabolism, reinforce the need to develop local delivery systems that optimize therapeutic effects and minimize undesirable systemic repercussions.

In this context, the incorporation of CBD into collagen membranes and *synthetic scaffolds* emerges as an innovative alternative to enhance ROG. Strategies such as hydrogels, biodegradable polymers, and microcapsules have been shown to be effective in providing controlled release, allowing continuous and localized exposure of bone tissue to the compound (BERNARDINI et al., 2018; KOZONO et al., 2010). This approach may be especially relevant in extensive bone defects or in patients with systemic regenerative

impairment, in whom the association between physical support and biochemical stimulation represents a possibility for optimizing clinical outcomes.

The literature also points to the synergistic potential of CBD when associated with other bioactive factors and regenerative therapies, such as bone morphogenetic proteins, growth factors, or mesenchymal stem cells, which can amplify its osteoinductive effects and create a microenvironment highly favorable to bone regeneration (LIU et al., 2019; GU et al., 2019). This multifunctionality highlights CBD as an agent with great potential to transform regeneration protocols in implantology and oral surgery.

Therefore, cannabidiol emerges as an innovative therapeutic alternative in guided bone regeneration, bringing together osteoinductive, anti-inflammatory, and analgesic properties that can enhance clinical results and reduce postoperative complications. The available literature suggests that modulating inflammation, stimulating osteogenic differentiation, and promoting tissue healing position CBD as a promising adjunct in regenerative procedures. However, relevant challenges for its clinical application remain, such as the definition of the optimal dosage, the most effective route of administration, the standardization of local delivery systems, and the rigorous evaluation of long-term safety. In addition, the scarcity of controlled clinical trials reinforces the need for investigations that validate preclinical findings and consolidate evidence-based protocols. In this scenario, deepening research on the integration of CBD into biomaterials and GBR membranes may not only expand the therapeutic arsenal of contemporary implant dentistry, but also contribute to improving the quality of life of patients undergoing oral surgical procedures (JIRÁSEK et al., 2022; KLEIN et al., 2018).

2 METHODOLOGY

The present research adopts the methodology of literature review as a central approach, since this strategy allows a critical and systematic analysis of the existing scientific production on cannabidiol (CBD) and its influence on guided bone regeneration (ROG), with direct implications for contemporary implantology. The literature review is widely used in biomedical and dental research, as it enables the synthesis of experimental and clinical data from different studies, providing a comprehensive view of physiological, pharmacological, and therapeutic mechanisms of bioactive agents, such as cannabinoids, in oral health and tissue regeneration contexts (BERNARDINI et al., 2018).

The methodological process followed a structured and careful approach, with defined steps for the selection, analysis, and interpretation of the evidence, ensuring rigor, reliability, and reproducibility of the findings. Initially, the objectives of the review were established: (i) to identify studies that investigated the effects of CBD and other cannabinoids on bone regeneration and periodontal healing; (ii) to analyze the cellular and molecular mechanisms involved in inflammatory and osteogenic modulation mediated by the endocannabinoid system; and (iii) to evaluate the clinical implications of these effects on implant dentistry, especially in the context of GBR.

The bibliographic search included databases of recognized academic relevance, including PubMed, PubMed Central and Taylor & Francis Online, ensuring the selection of peer-reviewed articles. The inclusion criteria covered publications between 2003 and 2023, involving *in vitro*, *in vivo*, and clinical trials that specifically addressed: (i) the effects of CBD or other cannabinoids on periodontal cells, periodontal ligament fibroblasts, osteoblasts, and osteoclasts; (ii) the modulation of inflammatory processes and tissue healing; and (iii) the impacts on guided bone regeneration and osseointegration in experimental and clinical models (ABIDI et al., 2020; GU et al., 2019; LIU et al., 2019). Studies with no direct relevance to dentistry, duplicates, or isolated case reports without robust experimental or clinical evidence were excluded.

The descriptors used included: *"Cannabidiol", "CBD", "endocannabinoid system", "bone regeneration", "guided bone regeneration", "periodontal healing*", *"oral wound healing"* and *"implant dentistry"*. The combination of the terms, associated with Boolean operators ("AND", "OR"), made it possible to refine the results and ensure the relevance of the selected studies. The final screening considered the careful reading of titles, abstracts, and full texts, ensuring that only publications of relevance to the defined objectives were included (JIRÁSEK et al., 2022; KLEIN et al., 2018).

The data analysis adopted an integrative approach, organizing the evidence into four thematic categories: (i) effects of CBD on periodontal inflammation and modulation of the local immune system; (ii) cellular mechanisms in osteoblasts and osteoclasts; (iii) impact of CBD on tissue adhesion, migration, and healing; and (iv) potential applications in guided bone regeneration, with emphasis on clinical implications for implantology. This categorization facilitated the correlation between experimental and clinical studies, allowing the identification of trends, gaps, and limitations in the literature (CARMONA RENDÓN et al., 2023; KONERMANN et al., 2017; KOZONO et al., 2010).

For the critical evaluation of the publications, methodological aspects were considered, such as experimental design, sample size, model used, type and concentration of cannabinoid administered, follow-up time, and histological, immunohistochemical, and molecular analysis methods. This methodological rigor allowed us to draw a reliable picture of the effects of CBD on bone regeneration and periodontal healing, highlighting promising results and pointing out inconsistencies between studies (NAKAJIMA et al., 2006; OSSOLA et al., 2020; WHYTE et al., 2012).

The included *in vitro* studies evidence CBD's ability to modulate inflammatory responses mediated by pro-inflammatory cytokines, such as interleukin-1β, in periodontal ligament fibroblasts, suggesting a protective effect during bone regeneration (ABIDI et al., 2020). In addition, research shows that the compound stimulates the adhesion and migration of periodontal and osteoblastic cells, reinforcing the role of the endocannabinoid system in bone remodeling and the integration of grafts in GBR (LIU et al., 2019; GU et al., 2019).

In vivo *studies* have revealed that the administration of CBD or CB2 receptor agonists promotes increased alveolar bone density and reduced bone resorption in experimental models of periodontitis in rats. CBD has also been observed to accelerate oral healing by promoting periodontal tissue regeneration and modulating the inflammatory response via NF-κB, one of the main signaling pathways for inflammation in periodontal tissues (KLEIN et al., 2018; NAKAJIMA et al., 2006; RAPHAEL-MIZRAHI; GABET, 2020).

The review also included studies on the toxicology and pharmacology of CBD, which are essential to assess its safety profile and clinical feasibility. According to Koturbash and Mackay (2020), the compound has low systemic toxicity and a favorable pharmacological profile, reinforcing its potential as an adjuvant therapeutic agent in GBR and implant dentistry. Additional evidence suggests that cannabinoids may act not only on bone regeneration, but also on reducing bacterial load on oral biofilms, creating a more favorable biological environment for implant osseointegration (STAHL; VASUDEVAN, 2020).

Thus, the methodology adopted in this review enabled a critical and integrated synthesis of the evidence on CBD and its application in GBR, highlighting molecular mechanisms, cellular effects, and potential clinical benefits for modern implant dentistry. Such an approach contributes to consolidating a robust body of knowledge, capable of supporting future clinical and experimental research, in addition to providing foundations for the incorporation of cannabinoid-based therapies into dental practice (PALLADINI, 2023; JIRÁSEK et al., 2022; CARMONA RENDÓN et al., 2023).

In short, the literature review was conducted in a structured, judicious and evidence-based manner, contemplating experimental, preclinical and clinical studies, with emphasis on the critical analysis of the effects of CBD on bone regeneration and periodontal healing. This methodology ensures that the conclusions presented here faithfully reflect the current state of scientific knowledge, providing relevant subsidies for clinical practice and for the advancement of guided bone regeneration techniques associated with the therapeutic potential of cannabidiol (BERNARDINI et al., 2018; KOZONO et al., 2010; RAPHAEL-MIZRAHI; GABET, 2020).

3 RESULTS

The analysis of the scientific literature on the impact of cannabidiol (CBD) on guided bone regeneration (GBR) reveals promising effects, both in modulating periodontal inflammation and in promoting osteogenesis, with potential applicability in implant dentistry. The reviewed studies demonstrate that CBD acts at multiple cellular and molecular levels, interacting with cannabinoid receptors (CB1 and CB2), modulating inflammatory pathways, and favoring the migration and adhesion of osteoblasts and periodontal fibroblasts, processes that are fundamental to the success of GBR (ABIDI et al., 2020; LIU et al., 2019; RAPHAEL-MIZRAHI; GABET, 2020).

3.1 MODULATION OF PERIODONTAL INFLAMMATION

Chronic inflammation is a critical factor that compromises bone regeneration in periodontal and implantological contexts. In this scenario, CBD has been shown to reduce the expression of pro-inflammatory cytokines, such as IL-1β, TNF-α, and IL-6, in periodontal ligament fibroblasts (ABIDI et al., 2020). This effect is primarily mediated by activation of the CB2 receptor, which triggers anti-inflammatory intracellular cascades, including inhibition of the NF-κB pathway (NAKAJIMA et al., 2006; GU et al., 2019).

In *vivo* studies in experimental periodontitis models in rats reinforce these findings, showing that CB2 stimulation reduces alveolar bone resorption, preserves bone height, and minimizes tissue destruction (OSSOLA et al., 2020; KONERMANN et al., 2017). In addition, CBD acts as an endocannabinoid modulator, regulating anandamide levels in gum tissue, which contributes to the suppression of exacerbated inflammatory responses (NAKAJIMA et al., 2006). This action is particularly relevant in GBR protocols, in which excessive

inflammation can compromise the integration of biomaterials and the osseointegration of implants.

3.2 PROMOTION OF OSTEOGENESIS AND CELL MIGRATION

CBD also has direct effects on osteogenesis. In *vitro* assays demonstrate that activation of cannabinoid receptors in osteogenic progenitor cells increases cell proliferation, adhesion, and migration, crucial steps for bone matrix deposition and initial vascularization in areas of bone defect (LIU et al., 2019; RAPHAEL-MIZRAHI; GABET, 2020).

Animal models confirm that local administration of CBD accelerates bone healing by stimulating collagen deposition and mineralization, with evident histological effects after two to four weeks of treatment (KLEIN et al., 2018). This effect is associated with the activation of the CB2-mediated PI3K/AKT pathway, which promotes cytoskeletal reorganization and focal adhesion of osteoprogenitor cells, favoring the integration of biomaterials and grafts into GBR (GU et al., 2019).

3.3 ANTIMICROBIAL EFFECT AND INFECTION PREVENTION

Another relevant finding is the antimicrobial effect of CBD, which indirectly contributes to bone regeneration by reducing bacterial load in periodontal and alveolar sites undergoing GBR. Preliminary studies have shown that CBD significantly reduces dental biofilm and the presence of periodontal pathogens, compared to commercial oral care products (STAHL; VASUDEVAN, 2020). The decrease in bacterial colonization creates a more favorable environment for osteogenesis.

This effect is in addition to the immunomodulatory action, as CBD can suppress exacerbated innate responses against oral pathogens through the CB2/PI3K axis (GU et al., 2019). This property is particularly useful in guided bone regeneration environments, in which the presence of pathogenic microbiota can compromise the integration of grafts and implants.

3.4 CLINICAL POTENTIAL IN MODERN IMPLANT DENTISTRY

The findings suggest that the local application of CBD in GBR protocols can optimize clinical outcomes in implant dentistry, especially in patients with chronic periodontitis or systemic conditions that affect osseointegration. Evidence indicates that CBD can be incorporated into graft biomaterials and barrier membranes, acting in a biphasic way:

stimulating osteogenesis and modulating inflammation (CARMONA RENDÓN et al., 2023; KOZONO et al., 2010).

In addition, studies have shown that CBD has a favorable safety profile, with minimal toxicity at therapeutic doses and a well-characterized pharmacological effect (KOTURBASH; MACKAY, 2020; BERNARDINI et al., 2018). The reduction of postoperative complications such as pain, excessive inflammation, and early bone loss reinforces the potential of CBD as an adjunct in guided bone regeneration protocols.

3.5 LIMITATIONS OBSERVED IN THE STUDIES

Despite the encouraging results, much of the evidence still comes from preclinical studies, carried out in animal models or cell cultures, limiting direct extrapolation to humans (JIRÁSEK et al., 2022). The heterogeneity in administration protocols, CBD concentrations, and duration of treatments also makes it difficult to standardize clinical recommendations.

Another relevant aspect refers to the complexity of CBD's interaction with receptors and metabolic pathways of the endocannabinoid system, which can vary according to factors such as age, inflammatory condition, and systemic status of the patient (MACCARRONE et al., 2003; PALLADINI, 2023). Thus, randomized clinical trials are still essential to confirm efficacy, determine safe doses, and define optimal forms of administration in humans.

3.6 FUTURE PROSPECTS

The results indicate that CBD has great potential as a modulator of guided bone regeneration, with promising applications in implant dentistry. Its incorporation into biomaterials, resorbable membranes, and bone grafts may represent an innovative strategy to improve healing, reduce inflammation, and prevent peri-implant bone loss (RAPHAEL-MIZRAHI; GABET, 2020; LIU et al., 2019).

Further investigation of the molecular pathways involved, such as CB2/PI3K, NF-κB, and endocannabinoid modulation, also paves the way for the development of combination therapies, integrating CBD with growth factors, morphogenetic proteins, or bone bioengineering techniques (KOZONO et al., 2010; GU et al., 2019). Such strategies can establish new paradigms in regenerative dentistry, especially for patients at increased risk of graft or implant failure due to chronic inflammatory processes.

In summary, the reviewed findings suggest that CBD exerts multiple beneficial effects on GBR, including modulation of periodontal inflammation, stimulation of osteogenesis,

increased cell migration and adhesion, and antimicrobial action. These combined effects reinforce the clinical potential of CBD as an adjunct in modern implant dentistry, representing a promising alternative to optimize the results of regenerative procedures and promote long-term oral health.

4 DISCUSSION

Guided bone regeneration (GBR) is an essential pillar in contemporary implant dentistry, especially in cases of alveolar bone atrophy, in which the preservation of bone volume and architecture is decisive for the success of the implants. In this scenario, there is growing interest in cannabidiol (CBD) as a biological modulator of the regenerative process, considering its anti-inflammatory, osteoprotective, and tissue healing promoting effects. Emerging literature indicates that CBD, the main non-psychoactive phytocannabinoid in *Cannabis sativa*, acts on the endocannabinoid system, modulating specific cellular responses in periodontal and bone tissues, which has direct implications for implantology.

The endocannabinoid system is composed of CB1 and CB2 cannabinoid receptors, endogenous endocannabinoids such as anandamide, and enzymes responsible for their synthesis and degradation. Evidence shows that the activation of the CB2 receptor promotes anti-inflammatory effects and regulates the activity of osteoblasts and osteoclasts, favoring bone homeostasis and regeneration in compromised tissues (WHYTE et al., 2012; RAPHAEL-MIZRAHI; GABET, 2020). In experimental models, CB2 stimulation prevented alveolar bone loss in early stages of periodontitis, suggesting a protective role in chronic inflammatory conditions (OSSOLA et al., 2020).

In the context of GBR, the reduction of local inflammation is determinant, since pro-inflammatory cytokines such as IL-1β and TNF-α can compromise the adhesion, proliferation, and differentiation of osteoblasts, impairing bone neoformation. CBD stands out for modulating critical inflammatory pathways, including inhibition of NF-κB activation in periodontal ligament fibroblasts, reducing the expression of inflammatory mediators (ABIDI et al., 2020; NAKAJIMA et al., 2006). This immunomodulatory effect contributes to a microenvironment that is more favorable to regeneration, promoting more efficient healing and reducing the risk of postoperative bone resorption.

In addition, CBD exerts a direct action on bone cell biology. In *vitro* studies indicate that CB2 activation by cannabinoid agonists stimulates the adhesion and migration of periodontal and osteoprogenitor cells, facilitating cell integration at the regeneration site (LIU

et al., 2019). This effect is relevant in GBR, where cellular colonization of the graft matrix is essential for the deposition of new bone tissue and the stability of the implants. In addition, research in animal models suggests that CBD accelerates oral healing, favoring re-epithelialization and vascularization of the underlying tissue (KLEIN et al., 2018), crucial steps for graft survival and the maintenance of osteogenesis.

The literature also points out that CBD modulates bone remodeling by regulating the activity of osteoclasts and osteoblasts. Whyte et al. (2012) demonstrated that endocannabinoids control the function of human osteoclasts *in vitro*, while Raphael-Mizrahi and Gabet (2020) showed that cannabinoids can stimulate bone formation and fracture healing. These findings reinforce that CBD not only attenuates inflammation, but also acts directly on bone neoformation, stimulating mineralized matrix deposition and potentially increasing peri-implant density.

Another relevant aspect is the interaction of CBD with the oral microbiome. Evidence suggests that CBD has significant antimicrobial activity against periodontal pathogens, such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, reducing bacterial load and, consequently, local inflammation (STAHL; VASUDEVAN, 2020; GU et al., 2019). This property contributes to a microenvironment that is more conducive to bone regeneration, minimizing the influence of infectious factors on the integration of grafts and implants.

Despite the promising results, important limitations should be acknowledged. Many studies still focus on animal or *in vitro* models, and clinical evidence in humans is incipient (CARMONA RENDÓN et al., 2023; JIRÁSEK et al., 2022). Extrapolation to clinical practice should be cautious, especially in patients with comorbidities or concomitant use of drugs that may interact with CBD (KOTURBASH; MACKAY, 2020). In addition, the pharmacokinetics of the compound, characterized by limited bioavailability, intense hepatic metabolism, and individual response variability, still need to be fully elucidated before its routine application in implant dentistry.

Another challenge concerns the route of administration and the optimal dosage of CBD. The literature suggests topical, systemic, and local possibilities, especially through incorporation into biomaterials and barrier membranes (KONERMANN et al., 2017; KOZONO et al., 2010). Clinical trials are needed to define dose-response, safety, and efficacy parameters, as well as to explore controlled-release systems capable of enhancing regenerative effects.

From a translational perspective, the use of CBD in ROG represents an innovative strategy that integrates biotechnology, pharmacology, and regenerative dentistry. The incorporation of cannabinoid-based therapies can transform clinical practice, especially in complex rehabilitation, in which the preservation of bone volume and the control of inflammation are critical factors for the longevity of implants (PALLADINI, 2023; BERNARDINI et al., 2018).

In summary, the discussion about the impact of CBD on GBR shows multiple mechanisms of action: (i) modulation of the inflammatory response via CB2 and NF-κB; (ii) stimulation of cell adhesion and migration; (iii) promotion of healing and revascularization; (iv) regulation of osteoblast and osteoclast activity; and (v) antimicrobial activity against periodontal pathogens. These effects converge to a microenvironment favorable to osseointegration and alveolar regeneration, providing scientific bases for the use of CBD as a therapeutic adjuvant in implantology.

Finally, it is highlighted that, although the body of evidence is encouraging, the clinical consolidation of CBD in GBR protocols requires large-scale randomized and controlled trials, capable of confirming its efficacy, safety, and optimal application protocols. In addition, legal and regulatory aspects must be considered, given that the use of cannabinoids in dentistry is subject to specific regulations that vary between countries (KOTURBASH; MACKAY, 2020). Thus, the translation of preclinical findings into clinical practice should be conducted with caution, but it presents itself as promising, opening new perspectives for regenerative dentistry and the advancement of modern implant dentistry.

5 CONCLUSION

The study of the impact of cannabidiol (CBD) on guided bone regeneration (ROG) demonstrates an innovative and rising therapeutic field in contemporary implant dentistry, with consistent evidence that this phytocannabinoid can act as a multifunctional agent in processes critical to the success of dental implants. The analysis of the literature shows that CBD is capable of modulating the inflammatory response, favoring osteogenesis, inhibiting bone resorption, and stimulating cell migration, composing a set of actions that reinforce its clinical applicability in alveolar reconstruction and oral rehabilitation scenarios.

From a biological point of view, cannabinoid receptor type 2 (CB2) activation emerges as one of the central mechanisms, regulating the expression of pro-inflammatory cytokines and contributing to periodontal and bone homeostasis. The suppression of the NF-κB

inflammatory pathway, the promotion of osteoblastic differentiation, and the inhibition of osteoclastogenesis configure a network of effects that favors the deposition of mineralized matrix and the preservation of peri-implant tissue. These findings have direct implications for the clinic, particularly in patients at increased risk of regenerative failure due to systemic conditions such as chronic inflammation and metabolic changes.

Additionally, the literature points to the contribution of CBD to tissue healing, vascularization, and control of the oral microbiota, aspects that increase its relevance as an adjuvant in regenerative protocols. The antimicrobial capacity of the compound, combined with its immunomodulatory action, reduces the bacterial load in surgical sites and favors the integration of biomaterials, which translates into a lower incidence of peri-implant complications. Thus, CBD is configured not only as a modulator of bone regeneration, but also as a potential protector against local infections, adding additional benefits to implantodontic practice.

However, it is necessary to recognize that most of the available studies still focus on experimental and preclinical models, and the clinical evidence in humans is limited. Aspects such as optimal dose, route of administration, bioavailability, and possible drug interactions remain poorly defined, requiring translational investigations and large-scale randomized controlled trials to confirm the efficacy and safety of CBD in dental settings. In addition, the methodological heterogeneity between the studies, with different administration protocols and concentrations used, highlights the need for scientific standardization to enable consistent comparisons and the formulation of applicable clinical guidelines.

In the regulatory and ethical sphere, the incorporation of CBD in guided bone regeneration protocols also demands attention. Despite its favorable safety profile, with low toxicity at therapeutic doses, the use of cannabinoids in health still faces social and legislative barriers, which vary according to the jurisdiction of each country. Overcoming these obstacles depends not only on the production of robust clinical evidence, but also on educational strategies aimed at health professionals, capable of expanding the acceptance of CBD as a legitimate and effective therapeutic resource.

In summary, the available scientific findings point to CBD as a promising tool to enhance guided bone regeneration, with benefits that include modulating inflammation, promoting osteogenesis, preventing bone resorption, and supporting tissue healing. The integration of this phytocannabinoid into the biomaterials and membranes used in GBR may inaugurate a new paradigm in regenerative implantology, especially in complex cases that

require more comprehensive therapeutic solutions. However, the safe translation of these results to clinical practice requires controlled and multicenter clinical studies, capable of establishing standardized and regulated protocols. The future of implant dentistry will thus be able to integrate cannabinoids, biotechnology and advanced surgical techniques, promoting greater predictability in treatments, reducing complications and improving the quality of life of patients undergoing complex oral rehabilitation.

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