

## USE OF CANNABIDIOL IN THE PREVENTION OF POSTOPERATIVE COMPLICATIONS AFTER THIRD MOLAR EXTRACTIONS

## USO DO CANABIDIOL NA PREVENÇÃO DE COMPLICAÇÕES PÓS-OPERATÓRIAS EM EXODONTIAS DE TERCEIROS MOLARES

## USO DE CANNABIDIOL EN LA PREVENCIÓN DE COMPLICACIONES POSTOPERATORIAS EN EXTRACCIONES DE TERCEROS MOLARES



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### ABSTRACT

Third molar extraction is among the most frequently performed procedures in Oral and Maxillofacial Surgery and is commonly associated with postoperative complications such as pain, edema, trismus, and functional limitation. In this context, cannabidiol (CBD) has attracted growing scientific interest due to its analgesic, anti-inflammatory, and endocannabinoid system-modulating properties, emerging as a potential therapeutic alternative for postoperative management in oral surgery. This study aimed to analyze, through an integrative literature review, the current scientific evidence regarding the use of cannabidiol in the prevention and control of postoperative complications associated with third molar extractions. The methodological framework was based on the stages proposed by

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Whittemore and Knafl (2005). The bibliographic search was conducted in the PubMed/MEDLINE, Scopus, Web of Science, and SciELO databases, considering studies published between 2015 and 2025 in English, Portuguese, and Spanish. Clinical trials, systematic reviews, observational studies, and experimental research related to the use of CBD in orofacial pain, inflammation, and oral surgery were included. The findings demonstrated that cannabidiol presents relevant analgesic and anti-inflammatory potential by modulating nociception and inflammatory responses through mechanisms associated with CB1 and CB2 receptors, in addition to reducing pro-inflammatory cytokines and nociceptive sensitization. Clinical studies reported reduction of postoperative pain, functional improvement, and possible reduction in the need for conventional analgesics. However, important methodological limitations remain, including heterogeneity among therapeutic protocols, differences in dosage and routes of administration, small sample sizes, and lack of clinical standardization. It is concluded that cannabidiol demonstrates promising therapeutic potential in the prevention and control of postoperative complications following third molar extractions, although further robust and standardized clinical studies are still required to consolidate its applicability in contemporary dental practice.

**Keywords:** Cannabidiol. Tooth Extraction. Third Molar. Postoperative Pain. Inflammation.

## RESUMO

A exodontia de terceiros molares está entre os procedimentos mais realizados na Cirurgia e Traumatologia Bucomaxilofacial, sendo frequentemente associada a complicações pós-operatórias como dor, edema, trismo e limitação funcional. Nesse contexto, o canabidiol (CBD) tem despertado crescente interesse científico devido às suas propriedades analgésicas, anti-inflamatórias e moduladoras do sistema endocanabinoide, configurando-se como potencial alternativa terapêutica no manejo pós-operatório em odontologia cirúrgica. O presente estudo teve como objetivo analisar, por meio de uma revisão integrativa da literatura, as evidências científicas atuais acerca da utilização do canabidiol na prevenção e no controle das complicações pós-operatórias associadas às exodontias de terceiros molares. A construção metodológica foi fundamentada nas etapas propostas por Whittemore e Knafl (2005). A busca bibliográfica foi realizada nas bases PubMed/MEDLINE, Scopus, Web of Science e SciELO, considerando estudos publicados entre 2015 e 2025, nos idiomas inglês, português e espanhol. Foram incluídos ensaios clínicos, revisões sistemáticas, estudos observacionais e pesquisas experimentais relacionados ao uso do CBD em dor orofacial, inflamação e cirurgia oral. Os achados demonstraram que o canabidiol apresenta potencial analgésico e anti-inflamatório relevante, atuando na modulação da nocicepção e da resposta inflamatória por meio de mecanismos associados aos receptores CB1 e CB2, além da redução de citocinas pró-inflamatórias e da sensibilização nociceptiva. Estudos clínicos indicaram redução da dor pós-operatória, melhora funcional e possível diminuição da necessidade de analgésicos convencionais. Entretanto, persistem limitações metodológicas importantes, incluindo heterogeneidade entre protocolos terapêuticos, diferenças de dose, vias de administração, tamanho amostral reduzido e ausência de padronização clínica. Conclui-se que o canabidiol apresenta potencial terapêutico promissor na prevenção e no controle das complicações pós-operatórias em exodontias de terceiros molares, embora ainda sejam necessários estudos clínicos mais robustos e padronizados para consolidação de sua aplicabilidade na prática odontológica contemporânea.

**Palavras-chave:** Canabidiol. Exodontia. Terceiro Molar. Dor Pós-Operatória. Inflamação.

## RESUMEN

La extracción de terceros molares es uno de los procedimientos más frecuentes en Cirugía Oral y Maxilofacial y Traumatología, y suele asociarse a complicaciones postoperatorias

como dolor, edema, trismo y limitación funcional. En este contexto, el cannabidiol (CBD) ha despertado un creciente interés científico debido a sus propiedades analgésicas, antiinflamatorias y moduladoras del sistema endocannabinoide, posicionándose como una potencial alternativa terapéutica en el manejo postoperatorio de la cirugía dental. Este estudio tuvo como objetivo analizar, mediante una revisión integradora de la literatura, la evidencia científica actual sobre el uso de cannabidiol en la prevención y el control de las complicaciones postoperatorias asociadas a las extracciones de terceros molares. La metodología se basó en los pasos propuestos por Whittmore y Knafl (2005). La búsqueda bibliográfica se realizó en las bases de datos PubMed/MEDLINE, Scopus, Web of Science y SciELO, considerando estudios publicados entre 2015 y 2025, en inglés, portugués y español. Se incluyeron ensayos clínicos, revisiones sistemáticas, estudios observacionales e investigaciones experimentales relacionadas con el uso de CBD en el dolor orofacial, la inflamación y la cirugía oral. Los hallazgos demostraron que el cannabidiol posee un potencial analgésico y antiinflamatorio relevante, actuando sobre la modulación de la nocicepción y la respuesta inflamatoria a través de mecanismos asociados a los receptores CB1 y CB2, además de reducir las citocinas proinflamatorias y la sensibilización nociceptiva. Los estudios clínicos indicaron una reducción del dolor postoperatorio, una mejoría funcional y una posible disminución de la necesidad de analgésicos convencionales. Sin embargo, persisten importantes limitaciones metodológicas, como la heterogeneidad entre los protocolos terapéuticos, las diferencias en la dosificación, las vías de administración, el tamaño reducido de la muestra y la falta de estandarización clínica. Se concluye que el cannabidiol presenta un potencial terapéutico prometedor en la prevención y el control de las complicaciones postoperatorias en las extracciones de terceros molares, aunque aún se necesitan estudios clínicos más sólidos y estandarizados para consolidar su aplicabilidad en la práctica odontológica actual.

**Palabras clave:** Cannabidiol. Exodoncia. Tercer Molar. Dolor Postoperatorio. Inflamación.

## 1 INTRODUCTION

Third molar extraction surgery represents one of the most performed procedures in Oral and Maxillofacial Surgery and Traumatology, and is often indicated in cases of dental impaction, pericoronitis, caries, root resorptions, periodontal alterations and prevention of future complications. Although widely performed and considered safe, it is a procedure associated with a significant postoperative inflammatory response, often accompanied by pain, facial edema, trismus, and functional limitation, factors that directly impact clinical recovery and quality of life of patients. The intensity of these complications may vary according to the surgical complexity, operative time, tissue trauma, and individual systemic characteristics of the patient (FERREIRA; RIBEIRO; MANDARINO, 2022).

In view of this scenario, different pharmacological strategies have been used with the aim of minimizing the inflammatory and painful repercussions resulting from extractions of third molars. Among the conventional approaches, nonsteroidal anti-inflammatory drugs and corticosteroids, especially dexamethasone and betamethasone, which are widely used in the prevention of postoperative edema, pain, and trismus, stand out. Recent studies have shown that the preemptive administration of these drugs presents satisfactory results in reducing inflammatory complications, especially when associated with multimodal analgesic protocols. However, adverse effects, clinical contraindications, and therapeutic limitations related to the prolonged or indiscriminate use of these drugs stimulate the search for safer and more effective therapeutic alternatives (GOMES JÚNIOR et al., 2025).

In this context, cannabidiol (CBD), a non-psychoactive compound derived from *Cannabis sativa*, has aroused growing scientific interest due to its analgesic, anti-inflammatory, anxiolytic and endocannabinoid system modulating properties. The endocannabinoid system plays an important role in modulating nociception, inflammatory response, and immune activity, acting through CB1 and CB2 receptors distributed in neural and peripheral structures related to pain control. Recent evidence suggests that CBD can reduce nociceptive sensitization, modulate pro-inflammatory cytokines, and contribute to the control of orofacial pain and inflammatory processes associated with the oral cavity, configuring itself as a potential therapeutic alternative in contemporary dentistry (TANGANELI et al., 2023).

In recent years, clinical studies and systematic reviews have begun to investigate the use of CBD in acute painful conditions related to dentistry, including spontaneous odontogenic pain and postoperative pain after tooth extractions. Randomized controlled trials have demonstrated significant pain reduction in patients undergoing oral use of CBD, as well as functional improvement related to bite force and possible decrease in the need for

conventional analgesics. In addition, recent reviews indicate that cannabinoids may exert favorable effects on oral inflammation, tissue edema, and bone healing, although the results still show methodological heterogeneity and limitations related to sample size, therapeutic standardization, and methodological quality of the available studies (CHREPA et al., 2024; CAMPANA et al., 2025).

Despite the advancement of research involving the therapeutic use of cannabidiol in dentistry, the scientific evidence currently available still remains limited, especially in the specific context of postoperative complications resulting from extractions of third molars. Although recent studies have demonstrated analgesic, anti-inflammatory, and nociceptive response modulating potential associated with CBD, the available results still show important methodological heterogeneity, including differences related to the formulations used, doses administered, routes of administration, therapeutic protocols, clinical outcomes evaluated, and patient follow-up time. In addition, there are still relevant gaps regarding the safety profile, therapeutic standardization, comparative clinical efficacy, and applicability of CBD compared to conventional pharmacological protocols employed in postoperative management in oral surgery.

In this context, the present study aims to analyze, through an integrative literature review, the current scientific evidence on the use of CBD in the prevention and control of postoperative complications associated with third molar tooth extractions, focusing on outcomes related to pain, edema, trismus, inflammation and functional recovery, seeking to contribute to the consolidation of more effective therapeutic approaches, safe and grounded in contemporary scientific evidence (WALCZYŃSKA-DRAGON et al., 2025; CARRASCOSA et al., 2024).

## 2 METHODOLOGY

This is an integrative literature review, developed with the objective of gathering, analyzing and critically synthesizing the available scientific evidence on the use of cannabidiol in the prevention and control of postoperative complications associated with extractions of third molars. The methodological construction of the study was based on the steps proposed by Whittemore and Knafl (2005), widely used in integrative reviews in the health area, contemplating the identification of the problem, definition of the search strategy, establishment of eligibility criteria, selection of studies, data extraction, critical analysis of the evidence and synthesis of the knowledge produced.

The main bibliographic search was performed in the PubMed/MEDLINE, Scopus, Web of Science and SciELO databases. Articles published between 2015 and 2025, in

English, Portuguese, and Spanish, were considered. Descriptors indexed in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) were used, including the terms "Cannabidiol", "CBD", "Third Molar", "Tooth Extraction", "Oral Surgery", "Postoperative Pain", "Edema", "Trismus", "Inflammation" and "Orofacial Pain", combined using the Boolean operators AND and OR. The search strategy was adapted according to the specificities of each database, seeking to increase the sensitivity of the identification of studies related to pain management, inflammation, and postoperative recovery in surgical dentistry.

Randomized clinical trials, systematic reviews, observational studies, review studies, and experimental research that addressed the use of cannabidiol or other cannabinoids in the management of pain, edema, inflammation, trismus, bone healing, and other postoperative complications related to surgical dentistry, especially in third molar extractions, were included. Studies focused on the endocannabinoid system and its participation in the pathophysiological mechanisms of orofacial pain were also considered, due to the relevance of these findings for understanding the possible therapeutic effects of CBD. Duplicate articles, studies without full text available, publications with insufficiently described methodology, studies without a direct relationship with the proposed theme, and studies directed exclusively to medical conditions unrelated to the dental context were excluded.

The selection of studies occurred in two stages. Initially, the titles and abstracts were read to identify potentially eligible works. Subsequently, the selected articles were submitted to full reading and critical analysis regarding thematic relevance, methodological consistency, and adequacy to the objectives of the review. During the evaluation of the studies, important limitations were observed related to the methodological heterogeneity of research involving CBD in dentistry, including differences between doses administered, routes of administration, pharmaceutical formulations, therapeutic protocols, and clinical outcomes analyzed, factors that hinder direct comparisons and limit the standardization of currently available evidence.

The data extracted from the included studies included information regarding the authors, year of publication, methodological design, study population, characteristics of the CBD intervention, route of administration, main outcomes evaluated, and results found. Subsequently, the findings were organized descriptively and submitted to critical qualitative analysis, allowing the construction of an integrative synthesis of scientific evidence related to the therapeutic potential of CBD in the prevention and control of postoperative complications in third molar tooth extractions, with emphasis on the effects on pain, edema, inflammation, trismus, and postoperative functional recovery.

### 3 RESULTS AND DISCUSSION

The studies included in this integrative review showed a progressive growth in scientific interest in the therapeutic application of cannabidiol (CBD) in the management of orofacial pain and postoperative complications associated with extractions of third molars. There was a predominance of systematic reviews, randomized clinical trials, experimental studies, and investigations related to the endocannabinoid system, with a main focus on pain modulation, inflammatory response, and postoperative functional recovery. Although a significant part of the literature is still composed of heterogeneous studies and small samples, current findings suggest relevant clinical potential of CBD as an adjuvant agent in the control of pain and inflammation in surgical dentistry (CAMPANA et al., 2025; WALCZYŃSKA-DRAGON et al., 2025).

Postoperative pain resulting from third molar tooth extractions is a direct consequence of surgical tissue injury, activation of peripheral nociceptors, and release of inflammatory mediators, including prostaglandins, bradykinin, substance P, and proinflammatory cytokines. In this context, the pharmacological mechanisms associated with CBD have shown a potentially favorable relationship with the modulation of these pathophysiological processes. The endocannabinoid system actively participates in nociceptive regulation through action on CB1 and CB2 receptors, distributed in central neuronal structures, peripheral nerve endings, and immune system cells. The indirect activation of these receptors by CBD seems to contribute to the reduction of nociceptive sensitization and modulation of pain transmission, in addition to influencing serotonergic receptors and TRPV1 channels involved in the perception of inflammatory and neuropathic pain (TANGANIELI et al., 2023; CARRASCOSA et al., 2024).

From a clinical point of view, the findings related to postoperative analgesia were particularly promising. The clinical trial conducted by Chrepa et al. (2024) identified a significant reduction in acute odontogenic pain in patients undergoing oral use of CBD, with progressive improvement in pain intensity and functional increase related to bite force. Similar results were observed in a recent pilot study involving post-tooth extraction pain, in which higher concentrations of CBD showed an analgesic trajectory qualitatively comparable to conventional therapy based on ibuprofen and acetaminophen, suggesting a possible sparing effect of traditional analgesics in certain clinical contexts (ABIDI; KASSAN; DEREFINKO, 2025).

In addition to nociceptive modulation, the results suggest an important role of CBD in the control of the post-surgical inflammatory response. Activation of the endocannabinoid system appears to reduce the production of pro-inflammatory cytokines, such as TNF- $\alpha$ , IL-

1 $\beta$ , and IL-6, as well as modulate inflammatory cell migration and oxidative stress associated with surgical trauma. These mechanisms are directly related to the pathophysiology of edema and trismus observed after extractions of third molars. Recent reviews have indicated that CBD can exert relevant anti-inflammatory effects on oral tissues and masticatory muscle structures, contributing to less functional limitation and improved postoperative recovery (CAMPANA et al., 2025; WALCZYŃSKA-DRAGON et al., 2025).

Although the literature specifically related to post-tooth extraction trismus still remains limited, studies involving orofacial pain, temporomandibular disorders, and muscle inflammation suggest that CBD may exert a favorable effect on muscle spasm and mandibular functional limitation. This effect is probably due to the reduction of peripheral inflammatory activity associated with the modulation of neuronal and muscular excitability. In clinical terms, this possible action becomes particularly relevant in surgeries of impacted third molars, in which muscle edema, surgical trauma, and limitation of mouth opening represent important factors of postoperative morbidity.

Another aspect discussed in the literature refers to the potential impact of CBD on healing and tissue repair. Experimental studies have shown that CB2 receptors can influence mechanisms related to bone remodeling, osteoblastic activity, and control of inflammatory bone resorption. Additionally, the antioxidant and immunomodulatory effects attributed to CBD seem to contribute to the reduction of local oxidative damage and modulation of the persistent inflammatory response. Although such mechanisms still lack robust clinical validation in surgical dentistry, current findings suggest a possible contribution of the endocannabinoid system to alveolar repair and post-tooth extraction tissue recovery (CAMPANA et al., 2025).

From a comparative perspective, CBD has potentially interesting pharmacological characteristics in relation to non-steroidal anti-inflammatory drugs and corticosteroids traditionally used in the postoperative period of tooth extractions. Although dexamethasone, betamethasone, and NSAIDs remain largely effective in reducing edema, pain, and trismus, their gastrointestinal, cardiovascular, metabolic, and renal adverse effects limit long-term use in certain patient groups. In this scenario, CBD emerges as a promising alternative within contemporary multimodal analgesia, especially due to the possibility of simultaneous action on pain, perioperative anxiety, and inflammation, without the typical psychoactive effects associated with tetrahydrocannabinol (THC). However, current evidence does not yet allow us to affirm therapeutic superiority over conventional pharmacological protocols, mainly due to the absence of robust and standardized comparative clinical trials.

Regarding therapeutic safety, the studies analyzed demonstrated a relatively favorable tolerability profile, with a predominance of mild and self-limiting adverse effects, including somnolence, mild gastrointestinal discomfort, xerostomia, and mild changes in taste. No serious complications related to the use of CBD were identified in the clinical studies evaluated. Even so, the literature highlights the need for caution regarding the pharmacokinetic variability of commercial formulations, differences in oral bioavailability, and possible drug interactions involving cytochrome P450-dependent hepatic metabolism (CARRASCOSA et al., 2024).

Despite the promising results, this review highlighted important methodological limitations in the currently available research. There was high heterogeneity among the studies regarding the doses administered, routes of administration, duration of use, pharmaceutical formulations, and clinical outcomes evaluated. In addition, many studies have shown small sample sizes, short follow-up periods, and lack of therapeutic standardization, factors that hinder more consistent clinical extrapolations. A significant part of the evidence still derives from experimental studies, narrative reviews, or investigations focused on general orofacial pain, not specifically directed at postoperative complications in extractions of third molars. Thus, although CBD demonstrates relevant therapeutic potential in modulating pain and postoperative inflammatory response, randomized clinical trials with greater methodological robustness are still needed, capable of establishing standardized therapeutic protocols, safe doses, and more reliable clinical parameters for routine application in surgical dentistry.

#### **4 CONCLUSION**

The use of cannabidiol in the context of third molar tooth extractions represents an emerging and potentially promising therapeutic approach for the management of postoperative complications associated with oral surgery. The evidence analyzed in this integrative review suggests that CBD may exert favorable effects on pain, inflammation, edema, and functional recovery, mainly due to its modulatory action on the endocannabinoid system, peripheral nociceptive mechanisms, and postoperative inflammatory response. In addition, their analgesic, anti-inflammatory, and anxiolytic properties reinforce the growing interest in the incorporation of cannabinoids into contemporary strategies of multimodal analgesia in dentistry.

The available findings also indicate that CBD has a relatively safe tolerability profile, with a low incidence of serious adverse effects in currently published clinical studies. However, despite the promising results, the evidence remains insufficient to consolidate

standardized clinical protocols for routine use in extractions of third molars. The literature shows important methodological heterogeneity, including differences related to the doses administered, routes of administration, pharmaceutical formulations, follow-up time, and clinical outcomes evaluated, in addition to the limitation due to small samples and scarcity of randomized clinical trials with greater methodological robustness.

Thus, it is concluded that cannabidiol emerges as a potential adjuvant alternative in the control of postoperative complications in third molar surgery, especially in the management of pain and inflammatory response. However, larger, standardized, and methodologically consistent clinical studies are still needed to better define its clinical efficacy, therapeutic safety, ideal dosage, and applicability in contemporary dental practice.

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