

# Cannabinoid therapy within the Unified Health System, perspectives in relation to pain treatment

*A terapia com canabinoides e perspectivas em relação ao tratamento da dor no Sistema Único de Saúde*

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## ABSTRACT

**BACKGROUND AND OBJECTIVES:** Pain is “an unpleasant sensory and emotional experience associated or not with real or potential tissue damage” which, when exceeding its protective function, beyond three months, is considered chronic pain, which in the long term can have its own clinical course. Given the scientific advances on the therapeutic effects of cannabinoids, the article brings a proposal for reflection as the Brazilian public health system (SUS – *Sistema Único de Saúde*), through medical cannabis, could offer better therapies for the treatment of conditions such as chronic pain.

**CONTENTS:** A narrative review was elaborated in databases such as Pubmed, Medline and Scielo. Considering the SUS Guidelines, the incorporation and access to medicinal cannabis can be understood as a strategy of social justice and reduction of inequities, because it is effective and safe in the treatment of chronic conditions, besides that the system already has strategies and policies aimed at regulating and distributing herbal medicines. Chronic pain is a prevalent condition, affects more than 2 billion people worldwide, and can be considered a global crisis. In Brazil, its prevalence varies between 23.02% and 76.17%, being higher in the elderly and female individuals. Despite this, in many cases, conventional treatments do not generate the analgesics effects expected, in addition to causing important adverse effects.

**CONCLUSION:** *Cannabis sativa* L. has great potential to become one of the best alternatives for chronic pain to be incorpo-

rated into herbal access programs around the country, such as in the SUS' *Farmácia Viva* project.

**Keywords:** Cannabinoids, Chronic pain, Complementary therapies, Delivery of health care, Phytotherapy.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS:** A dor é “uma experiência sensitiva e emocional desagradável associada, ou semelhante àquela associada, a uma lesão tecidual real ou potencial”, que, ao exceder sua função de proteção além de três meses é considerada dor crônica, e que em longo prazo pode ter seu próprio curso clínico. Diante dos avanços científicos acerca dos efeitos terapêuticos dos canabinoides, este artigo traz uma proposta de reflexão sobre como o Sistema Único de Saúde (SUS), por meio da medicina canábica, poderia ofertar melhores terapêuticas para o tratamento de condições que cursam com dor crônica.

**CONTEÚDO:** Foi elaborada uma revisão narrativa em bancos de dados como Pubmed, Medline e Scielo. Considerando as diretrizes do SUS, a incorporação e acesso a cannabis medicinal pode ser entendida como estratégia de justiça social e redução de inequidades, por ser eficaz e segura no tratamento de condições crônicas, além de que o sistema já conta com estratégias e políticas voltadas para regulamentação e distribuição de fitoterápicos. Dor crônica é uma condição prevalente, afeta mais de 2 bilhões de pessoas em todo o mundo e pode ser considerada uma crise global. No Brasil, sua prevalência varia entre 23,02% e 76,17%, sendo maior em idosos e em pessoas do sexo feminino. Apesar disso, em muitos casos, os tratamentos convencionais não geram os efeitos analgésicos esperados, além de causarem efeitos adversos importantes.

**CONCLUSÃO:** A *Cannabis sativa* L. tem um grande potencial de se tornar uma das melhores alternativas para dor crônica a ser incorporada nos programas de acesso a fitoterápicos no país, como no programa Farmácia Viva, do SUS.

**Descritores:** Canabinoides, Dor crônica, Fitoterapia, Prestação de cuidados de saúde, Terapias complementares.

## INTRODUCTION

Pain is “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”<sup>1</sup>, with a vital function in protecting the body. Pain exerts a protective function in animals, serving as an alert. This mechanism, with loss of its normal function, as in the case of post-surgical injuries, generates a painful symptom and re-

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## HIGHLIGHTS

- Medical cannabis discussed from a public policy perspective;
- Efficacy and safety of cannabinoids in chronic pain;
- Challenges and expectations concerning the inclusion of *Cannabis sativa* L. as a phytotherapeutic in the *Farmácia Viva* (Living Pharmacy) project and the Brazilian public health system (SUS – *Sistema Único de Saúde*).

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quires therapeutic interventions. It is important to have efficient therapeutic tools to handle this condition<sup>1</sup>.

Chronic pain (CP), for practical purposes, is considered to be pain that is persistent for more than three months. Thus, it loses its protective function and becomes a disease in itself. In the long term, it can also be the disease itself with its own clinical course<sup>2,3</sup>. It can also be independent of the causal event, without correlating in intensity with its causative agent, which may even be unknown<sup>2,3</sup>. Given the current scenario of indiscriminate use of opioids, data from 2018 already showed that around 30 million people abused these substances, causing many deaths. In the United States, this abuse is already considered an epidemic and a public health crisis and an alternative is increasingly needed to reduce this excessive consumption and avoid collateral damage. In this context, cannabis has significant relevance because it has a real potential to alleviate opioid withdrawal symptoms, reduce consumption, prevent relapse, and reduce overdose deaths<sup>4</sup>.

## THE ENDOCANNABINOID SYSTEM AND PHYTOCANNABINOIDS

Currently, much emphasis has been given to clinical medicine and research on the therapeutic effects of phytocannabinoids present in *Cannabis sativa* L., a plant whose molecules called phytocannabinoids can act effectively as analgesics, anti-inflammatories, anticonvulsants, anxiolytics, and even neuro-modulators. Cannabinoids act on the endocannabinoid system (ECS), an endogenous system recently discovered and described in the 1990's, which is responsible, among other functions, for homeostasis in vertebrate animals<sup>5-7</sup>. Many researches have directed their efforts to new pain treatments. One of the proposed mechanisms acts from the ECS modulation, in which exogenous cannabinoids coming from *Cannabis sativa* L also act. These discoveries were fundamental for elucidation of the phytocannabinoids mechanisms and places of action in pain modulation<sup>8-10</sup>.

Cannabidiol (CBD) is one of the best known phytocannabinoids. It has proven to be extremely versatile pharmacologically, also showing an analgesic effect, with action that may be responsible for suppressing neuronal excitability and pain perception<sup>11,12</sup>. Moreover, the other predominant phytocannabinoid, tetrahydrocannabinol (THC), also acts as a positive allosteric modulator of opioid receptors, suggesting the involvement of these receptors in the antinociceptive effect (drugs with analgesic potential) of both phytocannabinoids<sup>13-17</sup>.

### The dilemma of access to medical cannabis in Brazil

Access to medicinal cannabis in Brazil is still unequal, but it already happens for a small portion of the population, who seek this access through importation, patient associations, or even through judicial decisions for self-cultivation and artisanal production of the phytotherapeutic derivative. However, there is still the unofficial way, in which the majority still places themselves, assuming the risks inherent to the illegality of the substances, for lack of resources and the absence of the State in the regulation and distribution of the medicine<sup>18,19</sup>.

Through medical prescription, the treatment with phytocannabinoids is already regulated in Brazil, based on decisions taken by the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária* - ANVISA) in recent years. CBD, a phytocannabinoid whose therapeutic value arouses much scientific and commercial interest, was reclassified in 2015 and began to compose the class of controlled drugs on the C1 list of the Agency, subject to notification of special control prescription type B<sup>20</sup>. THC, the plant's psychotomimetic component, is still on the A3 list of psychotropic substances, subject to type "A" prescription notification<sup>21,22</sup>.

Given the advances in scientific knowledge of the therapeutic effects of cannabinoids, especially CBD and THC, this article brings a proposal for reflection on the strategies that could be adopted by the Brazilian public health system (SUS – *Sistema Único de Saúde*) in order to promote the health of the population, prevent injuries and complications and ensure access to the best therapeutic tools for treatment of chronic diseases, including CP, through cannabis medicine. In Primary Health Care (PHC), via the Family Health Strategy (ESF) as the gateway to the SUS, incorporating strategies such as Farmácia Viva (FV) – a national program that aims to rescue the use and potential of medicinal plants – and the Integrative and Complementary Practices (PIC) – national policy that uses therapeutic resources for prevention and health promotion, integrating the human being with the environment and society<sup>23-26</sup> – it would be possible to open paths for access to medical cannabis for social classes underprivileged, as it has been shown to be an effective therapy in improving living conditions linked to various diseases.

## CONTENTS

This study carried out a narrative review, searching for descriptors in international and national databases (Pubmed, Medline and Scielo portals), presenting an open theme, a selective literature review, without using a rigid protocol. This technique allowed the construction of the article in a more critical way, in order to comprehend the theme from a contextual point of view<sup>27</sup>.

## DISCUSSION

### SUS as a fair and universal public policy

During the 1980s in Brazil, after mobilizations around sanitary reform and the promulgation of the 1988 Constitution, SUS becomes the healthcare and sanitary model of public health. Art. 4 of Law n. 8,080 of 1990, which gives substance to public health policy in Brazil, defines it as "the set of health actions and services, provided by federal, state, and municipal public agencies and institutions, of the direct and indirect Administration, and foundations maintained by the Public Power"<sup>28</sup>. Among the services, actions, and interventions defined are care activities "for people, individually or collectively, aimed at the promotion and prevention, diagnosis, treatment, and rehabilitation of diseases and illnesses"<sup>29</sup>.

The incorporation and access to medical cannabis within SUS can be understood both as social justice and as a strategy to redu-

ce inequities, since it has already proven as effective and safe in the treatment of some diseases and very important in improving the life conditions of people such as those suffering from CP<sup>23,25</sup>. For a population that unequivocally can benefit from cannabinoid therapy, but that often tries it through unofficial or judicial means and without the accompaniment of a health professional, also because of the high cost of the products in Brazil, the access to medical cannabis by SUS becomes a fundamental action<sup>19</sup>. Strategies for access to herbal medicines are already a reality in Brazil through the National Policy on Integrative and Complementary Practices (PNPIC) and the National Policy on Medicinal Plants and Herbal Medicines (PNPMF) approved in 2006, which explore the medicinal power of the Brazilian flora, however without contemplating *Cannabis sativa* L. as a regulated plant for use in the SUS. All these practices offered by the SUS should preferably take place within the scope of the PHC and ESF, the gateway and organizational base of the Brazilian health system<sup>30-32</sup>. These are the foundations for implementation and regulation of medical cannabis, in order to guarantee access to services of promotion, protection, prevention, cure, rehabilitation, and palliative care throughout life, strategically prioritizing the main functions of the system aimed at individuals, families, and general population, effectively contributing to well-being and social insertion of citizens<sup>19,33,34</sup>.

Regarding phytotherapy, PNPIC offers to SUS users, within APS, the possibility of therapeutic use of plants *in natura* or dried (plant drug) and herbal medicines manipulated and/or industrialized. The responsibility for approval, regulation, and surveillance of these plant products lies with ANVISA, which has been improving the health legislation in order to meet the PNPMF and favor safe and free access to users<sup>35</sup>.

The use and distribution of medicinal plants and herbal medicines is subject to prescriptions from higher level health professionals, thus requiring continued education and preparation for them to use this therapeutic tool according to the Memento Phytotherapeutic of the Brazilian Pharmacopeia (*Memento Fitoterápico da Farmacopeia Brasileira - MFFB*), whose objective is to guide the prescription, oriented by scientific evidence, in addition to obtaining knowledge of identification, indications, posology, pharmaceutical presentation, precautions, and care with herbal medicines<sup>31,36,37</sup>.

A project that emerged in the 1980s, created by Professor Francisco José de Abreu Matos, from the Federal University of Ceará (*Universidade Federal do Ceará - UFC*), became, through the Ordinance n.º 866 of April 20, 2010, the FV<sup>38</sup>, creating a health service of pharmaceutical assistance linked to SUS to encourage and develop the practice of cultivation and distribution of herbal medicines. For it to work, the program needs agronomy professionals for cultivation and harvesting, pharmacy professionals to process, manipulate, and dispense the drugs, and professionals to prescribe it (doctors and dentists) who can guide the use<sup>39</sup>. Herbal medicines can enable the treatment for many of the diseases common in vulnerable communities, playing a very important role in public health<sup>40</sup>. These popular phytotherapy practices must be in line with good scientific practices in order to implement an effective

and efficient model, with resoluteness and benefits, ensuring free, equitable, universal, and integral access to the Brazilian population. Health managers must also encourage and develop scientific research with a critical view on the use of medicinal plants in SUS, including *Cannabis sativa* L.<sup>19,32,39</sup>.

### ***Cannabis sativa* L. as a therapeutic tool against pain**

CP affects about 2 billion people worldwide and is associated with impaired physical and emotional function, reduced participation in social and vocational activities, and lower perceived quality of life. CP prevalence varies within the medical literature, being estimated between 10% and 55% of the world population, with an average of 35%, predominantly in women, and whose most common locations are dorsal and lumbar spine<sup>1</sup>. In Brazil, a systematic review performed in 2021<sup>2</sup> confirms the trend presented by the International Association for the Study of Pain (IASP)<sup>41</sup>, showing prevalence ranging from 23.02% to 76.17%, presenting a national average of 45.59%<sup>43</sup>.

Data on the prevalence of CP in Brazil are scarce and can vary among regions; for example, 31% in Rio de Janeiro<sup>4</sup>, 76% in Maranhão<sup>2</sup>, 29.7% in São Paulo<sup>45</sup>, 26% in Florianópolis<sup>46</sup>, and 40% in Salvador<sup>47</sup>. Most studies show a higher prevalence in females, in people with advanced age (above 60% in people over 75 years old), being daily in almost 50% of the elderly, having moderate intensity for 45.8% of them and intense intensity for 46%, being associated with disabilities in daily and instrumental activities and with mobility alterations<sup>43,48</sup>.

CP can be considered a global health crisis due to its high prevalence and the high risk of progression to physical and emotional disability. Low back pain and neck pain are among the 10 leading causes of disability and functional leave in the world, causing enormous socioeconomic impact<sup>49</sup>. Among the main causes of disabling CP are musculoskeletal disorders, such as osteoarthritis. In Brazil, low back pain is among the five leading causes of disability<sup>50</sup>, with a prevalence around 40%, followed by pain in the upper and lower limbs and head and neck, and 15% report generalized pain. The high cost transferred to people and to State for the treatment of CP, associated with the functional and economic loss of people, justify the development of health policies for these cases, with scientific support and adapted to the epidemiological, socioeconomic, and cultural realities of each region<sup>42,51</sup>.

Through a population survey, a cross-sectional study conducted in Brazil presented alarming data such as that up to 15% of the respondents with CP did not even know the cause<sup>51</sup>. Regarding the treatments performed, almost half of the studied population reported “no effect” and only 14.9% as “very good” or “excellent”. Approximately 8% of the interviewees reported not having medical follow-up for the management of their pain.

Although acute pain can be considered adaptive, in some situations it evolves to chronic state, becoming a personal and public health problem. By generating a certain degree of physical and functional disability, temporary or permanent, dependence, and changes in family dynamics, the condition can bring high costs to health systems, with great impact on the patient and his family quality of life. Pain becomes the center of all ex-

periences, limiting decisions and behaviors. In addition, issues like social withdrawal, changes in libido, and feelings of hopelessness lead to other comorbidities such as anxiety, depression, and insomnia, among others<sup>52</sup>.

However, even with the negative CP impact on people's quality of life and its high prevalence and disabling power, traditional therapeutic tools often do not generate the expected analgesic effect and many of the drugs used cause significant adverse effects. Therefore, it is necessary to consider and use new forms of analgesia in CP treatment<sup>53,54</sup>.

The widely available analgesic agents are non-steroidal anti-inflammatory drugs (NSAIDs), COX inhibitors (cyclooxygenases), opioids, antidepressants, anticonvulsants, and anesthetics<sup>55</sup>. However, many of these drugs cause significant adverse effects, especially the opioids, which when used chronically can lead to increased tolerance, dependence, and risk of complications (even death from respiratory failure). Currently, opioids represent a major impact on mortality and morbidity, especially in the USA, where in recent years there has been an epidemic of indiscriminate use, with many associated deaths<sup>56</sup>.

In CP patients, treatment with medical cannabis has been associated with improved pain-related outcomes, increased quality of life, improved function and reduced need for opioid analgesia<sup>57</sup>. But despite being described and used for thousands of years, phytocannabinoids have only recently gained a more technical and evidence-based approach to use as medicines. These days, the pain management field is largely tilted toward research on cannabis-based drugs, and investigations continue to explore their potential medical benefits in relation to both cannabidiol (CBD) and THC (tetrahydrocannabinol)<sup>8,59</sup>.

## CONCLUSION

*Cannabis sativa* L. has potential to become one of the best therapeutic tools incorporated into programs to expand access to phytotherapies in Brazil through FV. The use of phytocannabinoids in clinical practice could expand the therapeutic arsenal of SUS professionals, so that it would be possible to reduce costs with production and/or supply of drugs in the public network, besides enabling a safe and efficient strategy to combat CP.

The incorporation of medical cannabis in SUS system can produce managerial and planning mechanisms for the promotion of health equity in groups which are in vulnerable situations, contributing to the institution of spaces for discussion on this topic. Although still very initial, with a conceptual and practical path to be followed, concerning strategies, policies and programs for its implementation, it is of fundamental importance that this theme be debated in all spheres of interest, from scientific development within academic institutions to political and governmental instances.

The insertion of medical cannabis in SUS system will require interdisciplinary articulations in order to promote health promotion, disease prevention, health surveillance, treatment and rehabilitation. Ensuring public funding for programs related to PIC, phytotherapies, and *farmácias vivas* ("living pharmacies"), continuing education for professionals, evaluation and

monitoring of results, and social participation are vital processes for the full implementation, planning, and programming of offering medical cannabis in the public health system in Brazil.

## AUTHORS' CONTRIBUTIONS

### Hygor Kleber Cabral Silva

Data Collection, Conceptualization, Research, Methodology, Writing - Preparation of the Original

### Rafaela Fernandes Lourenço

Data Collection, Methodology, Writing - Review and Editing.

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