

Therapeutic Uses of Cannabis: An Experience with an Elective Course to Introduce the Content in Undergraduate Medical Education

Usos terapêuticos da Cannabis: experiência de disciplina eletiva para introdução do conteúdo na graduação médica

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ABSTRACT

Introduction: Cannabis sativa L. has a thousand-year history of therapeutic use and scientific evidence of clinical applicability in conditions such as chronic pain, nausea and vomiting associated with chemotherapy, epilepsy and multiple sclerosis, in addition to growing evidence of a potential positive effect in several other morbidities. This great therapeutic potential, justified by the existence of a widely distributed endocannabinoid system with pro-homeostatic functions, is still little present in undergraduate medical school curricula.

Experience report: This report describes the elective course "Introduction to the Endocannabinoid System and the therapeutic use of Cannabis spp. and derivatives", offered in the third year of medical school at Botucatu School of Medicine of Universidade Estadual Paulista (FMB-UNESP). With a 30-hour workload and a hybrid format, the course brought together 32 students and addressed the Endocannabinoid System, product formulation, legal access routes and clinical practice.

Discussion: The initiative sought to fill gaps in medical training, considering the increased demand for the therapeutic effects of cannabis in Brazil.

Conclusion: The inclusion of the topic in medical undergraduate courses is essential to train future professionals in face of regulatory changes and emerging clinical needs.

Key-words: Medical Marijuana; Medical Education; Endocannabinoids.

RESUMO

Introdução: A Cannabis sativa L. possui histórico milenar de uso terapêutico e evidências científicas de aplicabilidade clínica em condições como dor crônica, náuseas e vômitos associados à quimioterapia, epilepsia e esclerose múltipla, além de crescentes evidências de potencial efeito positivo em diversas outras morbidades. Esse grande potencial terapêutico, justificado pela existência de um sistema endocanabinoide amplamente distribuído e com funções pró-homeostáticas, ainda é pouco presente nos currículos da graduação médica.

Relato de experiência: Diante disso, o presente relato descreve a disciplina eletiva "Introdução ao sistema endocanabinoide e ao uso terapêutico da Cannabis spp. e derivados", oferecida no terceiro ano de Medicina da Faculdade de Medicina de Botucatu da Universidade Estadual Paulista (FMB-Unesp). Com carga horária de 30 horas e formato híbrido, a disciplina reuniu 32 estudantes e abordou o sistema endocanabinoide, a formulação de produtos, as vias legais de acesso e a prática clínica.

Discussão: A iniciativa buscou suprir lacunas na formação médica, considerando o aumento da demanda pelos efeitos terapêuticos da Cannabis no Brasil.

Conclusão: A inclusão do tema na graduação médica mostra-se essencial para capacitar futuros profissionais perante as mudanças regulatórias e as necessidades clínicas emergentes.

Palavras-chave: Maconha Medicinal; Educação Médica; Endocanabinoides.

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INTRODUCTION

Cannabis sativa L. was one of the first plants domesticated by humanity, with evidence of cultivation approximately 12,000 years ago, in East Asia¹. The plant stands out for its morphological, phenotypic and chemical variability. Its possibilities of use range from nutritious food, biological fuel, resistant fiber or intoxicating resin, in addition to the extensive set of bioactive compounds and potential therapeutic applications². With such diverse uses, cannabis has a long history intertwined with the cultural, social, and economic development of diverse societies^{1,2,3}.

Regarding its use for health purposes, knowledge of the therapeutic applications of the plant dates back to approximately 2,700 BC, with its oral dissemination being attributed to the Chinese emperor Shen-Nung - considered one of the fathers of Chinese medicine - with subsequent compilation in the Pen-ts'ao Ching, the oldest known pharmacopoeia⁴. In ancient Egypt, papyri describe their use in the management of ophthalmological and gynecological conditions, fever, pain, and inflammation². In India, records date back to 1000 BC, when analgesic, anticonvulsant, hypnotic, tranquilizing, anesthetic, anti-inflammatory, antiparasitic, antispasmodic, aphrodisiac properties, among others, were already being explored⁴.

In modern Western medicine, the history of cannabis begins in the nineteenth century, with the application of the scientific method to the study of its pharmacological properties. The studies by O'Shaughnessy⁵ on the benefits of the use of cannabis tinctures in seizures, cholera, tetanus, and rabies stand out, already enrolled in the modern subdivision of preclinical pharmaceutical studies of safety and efficacy, followed by clinical trials⁶, while the contributions of Moreau⁷ focused on the psychoactivity of the plant and its potential application to fight symptoms related to mood disorders. Between the nineteenth and twentieth centuries, the literature highlighted a series of potential therapeutic uses of the plant, such as analgesic and hypnotic, appetite stimulant, antiepileptic and antispasmodic, prophylaxis and treatment of neuralgia, antidepressant and tranquilizer⁸.

From the 1960s onwards, the structures of the main phytocannabinoids present in the plant, cannabidiol (CBD)⁹ and delta-9-tetrahydrocannabinol (THC)¹⁰, were isolated and identified. Subsequently, studies identified endogenous cannabinoid receptors - CB1 and CB2 - on which phytocannabinoids and their synthetic analogues act, in addition to the endogenous ligands of these receptors - the endocannabinoids, mainly anandamide (AEA) and 2-arachidonylglycerol (2-AG)^{12,13}, as well as their synthesis and degradation enzymes, suggesting the existence of an Endocannabinoid System (ECS)¹⁴.

Evidence indicates the role of the ECS as an endogenous cell communication system with pro-homeostatic and pleiotropic functions, involved in the most diverse physiological and pathological processes¹⁵. The modulation of ECS activity has then been investigated as a potential therapeutic target for a wide spectrum of diseases, such as neurodegenerative, inflammatory, cardiovascular, metabolic, and pain, among others, although a deeper understanding of the complexity of this system is still necessary for the translation of this potential into clinical benefits¹⁶.

The path to scientific advancement in the therapeutic uses of cannabis was, however, limited by the international establishment of a prohibition regime initiated in 1961. The classification of the plant among particularly hazardous substances, being subjected to strict control, increased bureaucracy and the costs of obtaining it, with a consequent discouragement to scientific development or access as a treatment^{17,18}.

In addition to this institutional framework, which served as the basis for the promotion of a "War on Drugs" with enormous health and social costs^{19,20}, there was also the anti-cannabis propaganda initiated in the first decades of the twentieth century, which served political-economic interests and reproduced xenophobic and racist ideas, promoting stigmas that still persist^{21,22,23}.

In recent decades, however, a growing body of evidence has been relegitimizing the therapeutic potential of cannabis, associated with reforms in the regulation of the use in favor of the plant's health in several countries, especially in Europe and the Americas²⁴. Studies have already demonstrated a conclusive or substantial level of evidence for clinical use in conditions of chronic pain and neuropathic pain in adults, muscle spasticity in multiple sclerosis, chemotherapy-induced nausea and vomiting, and epilepsy as a symptom of rare genetic syndromes that affect children²⁵.

More recently, a mapping of the available evidence considering only high-quality studies has shown positive effects of cannabis for a substantial number of outcomes, such as patient safety, sleep quality, anxiety and cognitive disorders, in addition to the already known effects on seizures and epilepsy. In addition, potentially positive outcomes were observed for pain syndromes (chronic pain, cancer pain, and neuropathic pain), muscle spasticity, multiple sclerosis, substance withdrawal, and physical fitness, among others²⁶.

Despite the existence of considerable evidence, the therapeutic use of cannabis has little space in medical curricula. A survey conducted in the USA concluded that less than 10% of medical schools have the topic documented in their curriculum, indicating the existence of a knowledge gap in professional

training. The study also pointed out that 94% of students do not feel qualified to prescribe this therapy. The research concluded that education about cannabis use can make physicians more comfortable with the topic²⁷. The same was true among nursing students, who considered that education on the subject influenced their clinical practice²⁸.

There are similar challenges in Brazil. Although students recognize the therapeutic potential of cannabis, few have actually had contact with prescribing professionals, and its use is still incipient in Brazilian clinical practice²⁹. The deficit in the training and incorporation of this resource into the therapeutic arsenal is particularly relevant considering the growing demand in the country: more than 670,000 Brazilian patients used cannabis in 2024, an increase of 56% compared to 2023³⁰.

In this context, the low presence of the topic in medical curricula configures an insufficiency in the development of skills necessary for the understanding of scientific advances, guidance and clinical management of patients³¹. Aiming to create solutions for this scenario, an elective course was developed to introduce the topic in the third year of the medical undergraduate course, at the Botucatu School of Medicine of Universidade Estadual Paulista (FMB-UNESP).

EXPERIENCE REPORT

The present report reflects the experience of the faculty regarding the creation and implementation of a multidisciplinary pedagogical project for the introduction of content related to the ECS and the therapeutic uses of cannabis, at the undergraduate level in health, as well as a discussion about the relevance of the presence of this content at this moment of training. It is a qualitative description of the training process carried out with medical students from FMB-Unesp, who participated over the course of eight weeks of the elective course “Introduction to the Endocannabinoid System and the therapeutic use of *Cannabis* spp. and derivatives”, together with a faculty whose areas of activity covered neurosciences, collective health, law, bioethics and psychiatry. The construction of the course program, which is summarized in table 1, had as its main objective to present the rationality underlying the therapeutic uses of the plant combining perspectives from different fields of knowledge, introducing the historical and ethnobotanical aspects related to use, the physiological and pharmacological foundations of the modulation of the ECS as a therapeutic target, the therapeutic indications of cannabis and the ethical, legal, clinical and sanitary aspects related to prescription and access to cannabis-based medicines. The discipline took place in a hybrid format, with seven face-to-face meetings and a remote one, through

Chart 1. Course schedule.

Week 1	Historical aspects related to the therapeutic use of cannabis, prohibition policies and relegitimization.
Week 2	Introduction to the endocannabinoid system and the plausibility of its modulation as a therapeutic target
Week 3	<i>Cannabis sativa</i> L.: botanical and pharmacological aspects and the biopsychosocial understanding of its therapeutic uses.
Week 4	Medicinal quality cannabis: product composition and quality defining criteria for cannabis-based products.
Week 5	Forms of legal access to cannabis-based products in Brazil. Social impacts of the national drug policy.
Week 6	Fundamentals of clinical practice with cannabis-based products. Clinical case discussion: therapeutic use in chronic pain.
Week 7	Therapeutic use of cannabis and derivatives in the treatment of Autism Spectrum Disorder (ASD): clinical case discussion.
Week 8	Therapeutic use of cannabis and derivatives in complex genetic and neuropsychiatric conditions: clinical case discussion.

the Google Meets platform. The course had a workload of 30 hours and was offered as an elective to 32 students in the 3rd year of medical undergraduate course, in 2024.

The reported experience does not involve the students enrolled in the course individually, reflecting the analysis of pedagogical practices in the perception of teachers and collaborators of the discipline. No direct data collection was carried out for the preparation of this text. The project was submitted to the Research Ethics Committee (CEP) of the Botucatu School of Medicine and duly approved: Certificate of Presentation for Ethical Appreciation (CAAE) N. 86506825.3.0000.5411.

The schedule of the elective course was based on the following topics:

Week 1

Opening class “Medicinal Cannabis: museum of great novelties”. In this first meeting, the historical aspects related to the therapeutic uses of cannabis and the historical evolution of the discoveries that founded the rationale for the therapeutic use of the plant^{1,2,3} were addressed, denoting the existence of an ECS¹⁴. The scientific advance represented by the isolation of the main cannabinoids and the discovery of the ECS was countered by the international regime for the prohibition of psychoactive substances and the anti-cannabis propaganda policies, which created bureaucratic, financial,

and moral obstacles to the use of the plant for medical and scientific purposes^{19,20,21,23}.

Week 2

Theoretical class “The endocannabinoid system and the fundamentals of its modulation as a therapeutic target”. The students were introduced to cannabinoid receptors (CB1 and CB2), their distribution in the human body, the endocannabinoids AEA and 2-AG, and their synthesis and degradation enzymes. The existence of other receptors modulated by endogenous cannabinoids and phytocannabinoids, such as G-protein-coupled receptors, ion channels, and nuclear receptors, was also introduced^{10,11,12,13}. The classic action of endocannabinoids as retrograde signaling in the CNS and the possibilities of their action directly on postsynaptic neurons, or mediated by astrocytes, as well as the on-demand production of endocannabinoids, correlating it to the pro-homeostatic function of the ECS, were presented. Finally, the action of the ECS on development, spatial memory, extinction of aversive memories and fear conditioning; anxiety and mood, eating behavior, reward, pain, and the immune system was addressed^{14,15,16}.

Week 3

Theoretical class “*Cannabis* spp. and its therapeutic action”, with an introduction to the morphology and physiology of cannabis, the main derivatives of its secondary metabolism (phytocannabinoids, terpenes and flavonoids), taxonomy and biochemical characterization of cannabis variants³². The pharmacological action of synthetic cannabinoids and phytocannabinoids on cannabinoid receptors and other neurotransmission systems and the synergism proposed for the joint action of the plant derivatives – the entourage effect – was also introduced³³. Finally, the effects of cannabis were discussed from a biopsychosocial perspective, evidencing the interaction between the physiological effects of the plant, the user’s psychological state and the social context in which the use is inserted^{20,21}.

Week 4

In the theoretical class “Medicinal quality cannabis”, the types of cannabis products were presented – full spectrum, broad spectrum, isolated cannabinoids, synthetic products and synthetic analogues³⁴. The therapeutic action profile and side effects of the different formulations were discussed, contrasting the behavior of the isolated products with the combined ones³⁵. The possibility of variation in the expression of phytocannabinoids and the need for standardization of extracts to maintain therapeutic effects were addressed. Finally, the determinants of the quality of a cannabis

product were presented, such as the presence of a certificate of analysis, preferably from an independent laboratory, communicating batch, concentration of cannabinoids, composition of the product, and absence of chemical and biological contaminants³⁶.

Week 5

Theoretical class “Forms of legal access to cannabis in Brazil”, taught by a guest jurist, presenting the Brazilian regulation of therapeutic and adult uses of cannabis. The prohibition of the “Pito do Pango” in 1830, the criminalization in 1932 and the Drug Law of 2006^{19,20,21} were addressed. A critical discussion was held about the penalization centered on the black, poor and peripheral population in the implementation of these laws. RDCs (Collegiate Board Resolutions) 327/2019³⁷ and 660/2022³⁸ established by Anvisa were also presented, and the requirements for granting health authorization to obtain cannabis products were discussed, as well as requirements for marketing, prescription, dispensation and monitoring, and the process of importing them for health treatment. The students were introduced to associativism and its operation in the cultivation and supply of cannabis-based products, in addition to the figure of preventive *Habeas Corpus*, with the purpose of safe conduct for the cultivation of cannabis for therapeutic use³⁹.

Week 6

Class entitled “Fundamentals of clinical practice with cannabis-based products.”, with a meeting held remotely. The students came into contact with the different routes of administration of cannabis-based products (oral, topical, nasal, inhalation, vaginal, rectal), main types of oils (full spectrum, broad spectrum and isolated CBD), and the entourage effect on the action of phytocannabinoids was also revisited^{33,35}. Also in focus was the need to align expectations with patients, the evaluation of their demands, indications, medical prescription, doses, dose adjustment and therapeutic follow-up. At the end of the discussion, there was a presentation and discussion of the prescription in a clinical case of chronic pain³⁵.

Week 7

Class entitled “Clinical use of medical cannabis in mental health: Autism Spectrum Disorder (ASD)”. The first part of the class focused on understanding the signs and symptoms of ASD, as well as the diagnosis and treatments established by the literature^{40,41}. Subsequently, a clinical case refractory to conventional medications was presented to and discussed with the students, highlighting the substantial improvement in behavioral symptoms and quality of life of the patient and family after the introduction of cannabis in the prescription.

Week 8

Class entitled “Cannabidiol: light in clinical complexity”. In this last meeting, a clinical case of a patient with Smith-Magenis genetic syndrome, as well as epilepsy and Autism Spectrum Disorder level 3^{40,41,42} was discussed. Previous therapeutic failures, caregiver overload, difficulties in patient behavioral management, and the introduction, dose management, and safety control of medical cannabis prescription as a therapeutic option were the topics addressed³⁵.

As a closing, there was a discussion with the students to identify their perceptions about the topics of the discipline and its approach. The evaluation was carried out through a critical review, aiming to analyze the assimilation of the addressed concepts, and the students’ perceptions and attitudes about the therapeutic use of cannabis. As instructions, students were advised to reflect on their previous knowledge and contact with the covered topics, summarize the main learnings about the therapeutic use of cannabis and its indications, and evaluate the relevance of the presence of the content in the medical undergraduate course.

DISCUSSION

The use of *Cannabis sativa* L. as a therapeutic resource has been transmitted and recorded in different medical systems and cultures since before the beginning of the Christian Era. In recent decades, the discovery of the ECS and the wide range of potential clinical uses of the plant, and the activism of patients, families, and professionals have subsidized reforms of prohibitionist regulatory policies, which for more than half a century have created obstacles to the advancement of the use of cannabis in medicine^{16,24}.

After decades of bureaucratization, scientific backwardness and stigmatization, the plant returns to pharmacopoeias⁴³, research and clinical practice without educational institutions having incorporated this knowledge into professional training. Thus, the lack of knowledge on the subject constitutes a new obstacle to the development of policies involving the therapeutic application of cannabis⁴⁴, with studies showing that the difficulty in finding a physician to support the demand for treatment is one of the barriers to access in countries that have proposed regulatory reforms⁴⁵.

Likewise, insufficient knowledge about the therapeutic and adverse effects, as well as difficulties in guiding patients, seem to constitute barriers to the prescription of cannabis and derivatives, and it is necessary to deepen the study of the factors that facilitate or enable prescriptive practice^{46,47,48}.

Thus, it is relevant to recognize the need to introduce the topic in medical education while in undergraduate courses,

considering that the demand is not only directed to specialists, the diversity of clinical conditions whose modulation of the ECS can benefit, advances in health regulation and the growing scientific production.

FINAL CONSIDERATIONS

It is expected that health professionals will be faced with the demand for the therapeutic use of cannabis and derivatives in their professional practice. They must therefore be able to discriminate the best indications for treatment, provide guidance on expected benefits and adverse events, and understand the elements that define the quality of a cannabis-based product. It is also important that they know how to deconstruct stigmas related to therapy, clearly agreeing on expectations of results and formulating singularized strategies for each clinical case.

The central role of undergraduate health courses in the construction of a qualified response to the demand for cannabis treatments is highlighted, so is the need to introduce the topic in the medical training curriculum. In this sense, the experience of introducing an elective course in the third year of the undergraduate course in Medicine fulfilled the role of paving the way for a necessary curricularization of the content related to the ECS and the therapeutic uses of cannabis, promoting a didactic experience and seeking the collaboration of the student body to evaluate and qualify the introduction of the content in the undergraduate course in health.

AUTHOR CONTRIBUTIONS

Marcelo Colombini Ranieri contributed with conceptualization, research, methodology and writing - original draft. Julia Pellizon Mazucco contributed with writing - original draft. Heloísa Scattone contributed with methodology and writing - review and editing. Pedro Nicoletti contributed with methodology and writing - review and editing. Renato Filev contributed with methodology and writing - review and editing. Débora Gomes-Medeiros contributed with conceptualization, research, methodology, project administration, supervision and writing - original draft.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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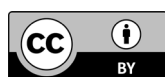
DATA AVAILABILITY STATEMENT

Research data is available in the body of the document

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