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Medical cannabis: Exploring therapeutic perspectives and regulatory context

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Abstract

The utilization of medical cannabis, specifically the therapeutic potential of cannabinoids, has garnered significant attention in recent years. This literature review aims to delve into the intersection between therapeutic perspectives and the regulatory context surrounding medical cannabis. Key terms such as medical cannabis, cannabinoids, regulation, chronic pain, and multiple sclerosis (MS) will be explored to provide a comprehensive understanding of the subject.

Therapeutic applications of medical cannabis will be examined, with particular focus on its potential in managing chronic pain and alleviating symptoms associated with multiple sclerosis. Furthermore, the complex regulatory landscape surrounding medical cannabis will be analyzed, taking into account various legal frameworks, guidelines, and constraints imposed by governing bodies.This article highlights emerging scientific evidence supporting the use of medical cannabis, including the efficacy of cannabinoids in pain management and their impact on multiple sclerosis symptoms. Additionally, it will address the challenges faced by healthcare professionals, patients, and policymakers due to varying regulations across jurisdictions.

Keywords: Medical cannabis; Cannabinoids; Regulation; Chronic pain; Multiple sclerosis

1. Introduction

Globally, *Cannabis sativa L*, Cannabaceae, or hemp, is the most widely consumed drug, with an estimated number of users reaching 200 million in 2021 [1,2].

The medical use of cannabis dates back over 5,000 years in China [3]. Over time, it spread throughout Asia, the Middle East, and Africa [4]. However, since the emergence of AIDS in the 1980s, cannabis has experienced a renewed interest, particularly for its ordemandic, antiemetic, and analgesic properties.In recent decades, there has been a resurgence of support for its decriminalization and legalization for medical purposes, driven by new scientifically based indications of its potential therapeutic value [5].

On December 2, 2020, the United Nations Commission on Narcotic Drugs (CND), the decision-making body of the UN for drug control, reclassified cannabis and cannabis resin in an international list that recognizes its medical value.

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Figure 1 *Cannabis sativa L*, Cannabaceae [6]

The objective of this study is to gather, analyze, and organize multiple articles and scientific content to provide an overview of advancements in the therapeutic and regulatory aspects of medical cannabis.

2. Material and methods

A literature search was conducted on search engines such as Google Scholar, PubMed, and Sci Finder, focusing on clinical trials involving medical cannabis, literature reviews, non-clinical trials, and articles on non-medical cannabis use.

The main keywords used were medical cannabis, clinical trials, medical and therapeutic uses, psychotropic, and legislation.

After the selection of publications, the countries of origin were identified to assess the current regulations in each of them regarding medical cannabis.

The scientific literature and relevant official publications from government and local authorities were consulted for this analysis. Additionally, the characteristics and results of clinical studies were analyzed to assess any potential links with the legislation of the state where the studies were conducted.

3. Results and discussion

3.1. Pharmacological Aspects and Therapeutic Perspectives

3.1.1. The Endocannabinoid System

The endocannabinoid system (ECS) comprises a set of receptors present throughout the human body. This system reacts to endogenous molecules, created within the body, that activates the same receptors as cannabis by binding to cannabinoid receptors. Two receptors of the endocannabinoid system have been isolated: the CB1 receptor, which primarily acts in the nervous system, and the CB2 receptor, which has an effect on immune system cells [7].

The mechanisms of action and pharmacokinetics of cannabis are primarily related to delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Both THC and CBD bind to the CB1 and CB2 cannabinoid receptors of the endocannabinoids in the body[8] [9].

When THC, with a high affinity for the CB1 receptor, enters the bloodstream and reaches the brain, it binds to cannabinoid receptors. The endogenous ligand of these receptors is anandamide, whose effects THC mimics. This agonist of cannabinoid receptors leads to changes in the levels of various neurotransmitters, particularly dopamine and norepinephrine, neurotransmitters closely associated with the acute effects of cannabis ingestion, such as euphoria,

anxiety, sometimes a general alteration of consciousness, relaxation, stress reduction, and increased creativity. This is what makes THC a psychoactive substance[8] [9].

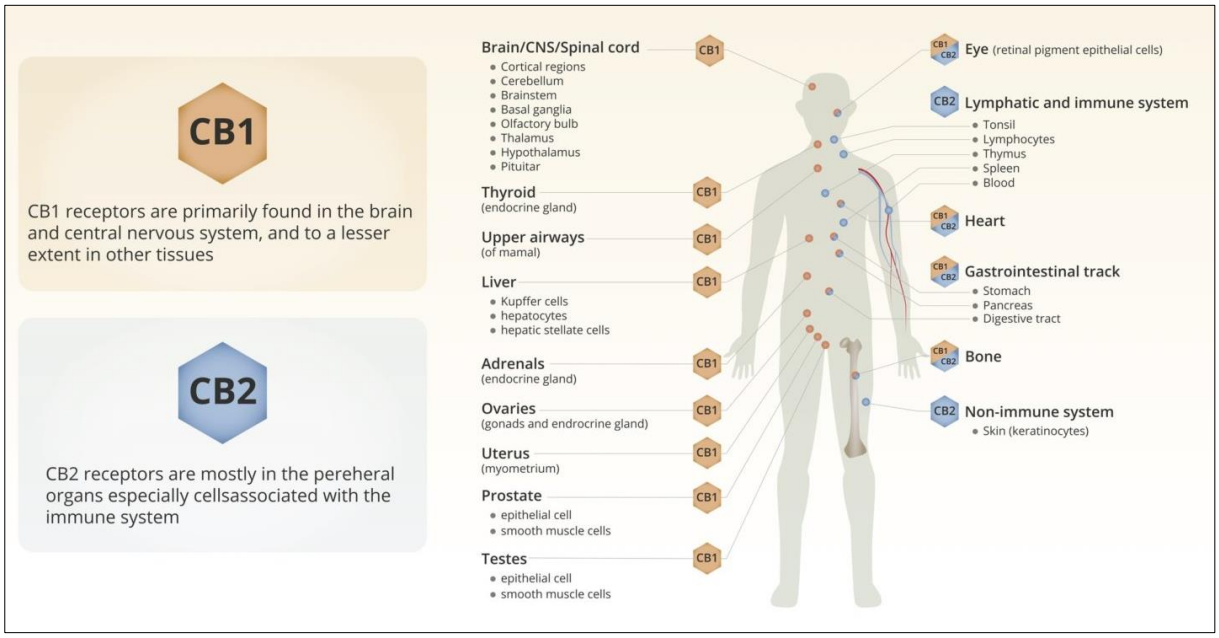

Figure 2 Endocannabinoid system receptors (CB1 & CB2) [7]

CBD, on the other hand, has several pharmacological targets. It has low affinity for the CB1 receptor, unlike THC, which explains the absence of psychoactive effects. CBD acts on serotonin (5HT1A) receptors, dopamine D2 receptors, GABA receptors, as well as glutamatergic systems, which may explain certain neurological effects such as sedation, drowsiness, and anticonvulsant effects [8] [9].

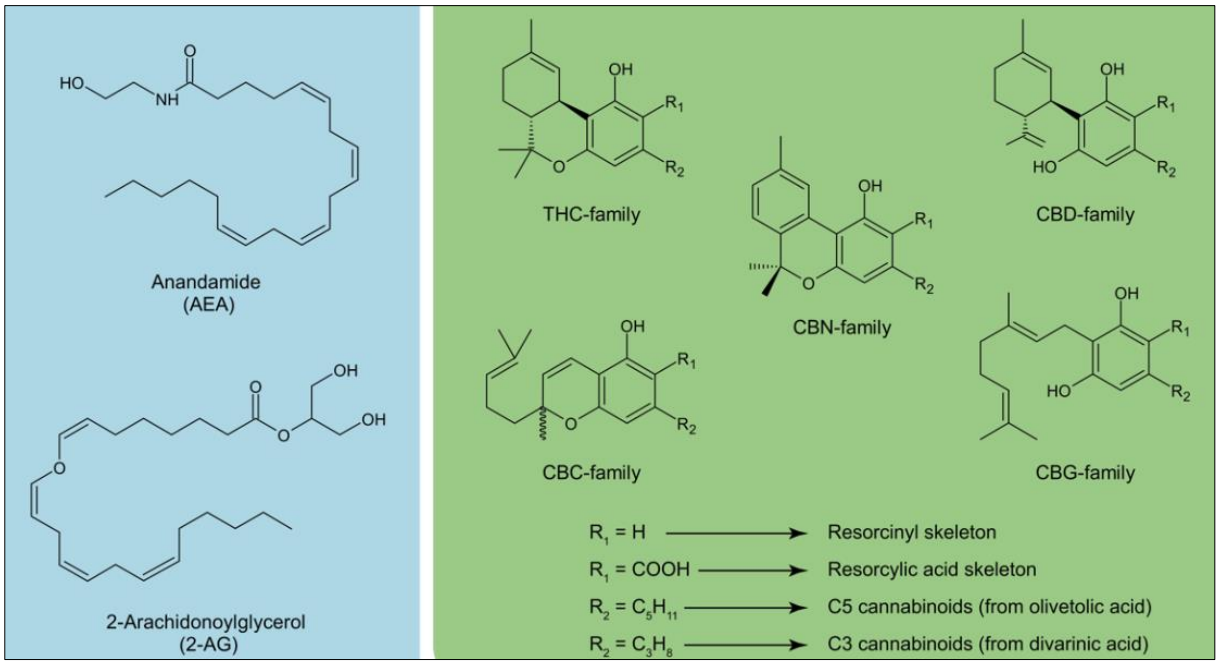

Figure 3 Endocannabinoids versus Phytocannabinoids [13]

Currently, 104 molecules have been identified belonging to the class of cannabinoids [10]. These molecules are divided into 11 subcategories, including THC and CBD.

Tetrahydrocannabinol (THC) is the main psychotropic component of cannabis. It is a partial agonist of CB1 and CB2 receptors, as well as an agonist of PPAR-g receptors (involved in cellular glucose regulation, protection against atherosclerosis, and immune response control) and TRPA1 receptors (involved in nociception) [11].

Cannabidiol (CBD) currently has the most potential therapeutic indications, with the advantage of not having the psychoactive side effects of THC. In terms of metabolism, it is almost identical to that of THC. However, CBD is a low-dose antagonist of CB1 and CB2 receptors, which helps reduce the psychoactive effects of THC when administered together. Additionally, it exerts many of its pharmacological effects through other receptors [12].

There are now several cannabinoid products available for medical use worldwide:Dronabinol: Synthetic THC in the form of an oral pill, marketed as Marinol®.Nabilone: A synthetic derivative of THC in the form of an oral pill, marketed as Cesamet®.Nabiximols: A standardized extract from a cannabis strain containing equal proportions of THC and CBD, marketed as Sativex® [10,11,12].

3.1.2. Therapeutic Applications of Medical Cannabis in Certain Severe Conditions:

Cannabis in Chronic Pain States

Chronic pain and neuropathic pain have a small number of indications for which there is substantial evidence supporting the effectiveness of medical cannabis pharmacotherapy. Several studies have shown that cannabis can be an effective pharmacotherapy for pain and neuropathic pain.

The efficacy of cannabis in pain treatment was initially demonstrated in preclinical studies, suggesting that the endocannabinoid system plays an active role in pain control. Animal models of pain have been used to support this hypothesis. Delta-9-tetrahydrocannabinol (THC) has been shown to produce analgesic and anti-hyperalgesic effects in mice[14]..

These analgesic effects have been anecdotally confirmed in patients suffering from chronic pain, and numerous clinical studies have aimed to investigate these effects in human models.

Whiting et al. conducted a systematic review and meta-analysis of randomized clinical trials on cannabis and cannabinoids[14]..

This review analyzed 28 studies evaluating chronic pain in a total of 2,454 participants. Overall, there was a higher reduction in pain measures with cannabinoids compared to placebo, but most of these differences were not significant in each study[14].

A recent report published by the National Academy of Sciences, Engineering, and Medicine in the United States stated that there is "conclusive or substantial evidence" that cannabis or cannabinoids are effective treatments for chronic pain[14].

Furthermore, another review determined that there is "high-quality evidence," as demonstrated by several positive placebo-controlled randomized trials, to support the administration of cannabis or cannabinoid pharmacotherapy for the treatment of chronic pain and neuropathic pain [14].

Some clinicians consider the analgesic effect of cannabis to be insufficient to offset its adverse effects (Saxon and Browne, 2014).

Cannabis in Multiple Sclerosis

As of October 2017, there had been at least 14 randomized clinical trials aimed at demonstrating the effectiveness of cannabis treatment for spasticity associated with multiple sclerosis. Many of these studies have shown that cannabis or cannabinoids were helpful in relieving spasticity.

The American Academy of Neurology found these results promising, leading to the publication of evidence-based guidelines for physicians recommending an oral cannabis extract containing both THC and cannabidiol (CBD) for the treatment of spasticity and pain associated with multiple sclerosis.The most commonly alleviated symptoms by cannabis were muscle stiffness, spasticity, and sleep disturbances [09].

Cannabis in Cancer

Available literature suggests that the endocannabinoid system could be targeted to suppress the progression and advancement of breast, prostate, and bone cancers, as well as the accompanying pain syndromes. Activation of the endocannabinoid signaling system produces anticancer effects in other types of cancer, including skin, brain (gliomas), and lung (Velasco et al., 2007; Bíró et al., 2009; Pacher and Mechoulam, 2011 for reviews).

However, the results of fundamental research are far from being fully understood, and further research is needed to better understand the complexity of the dynamic changes in the endocannabinoid system in cancer. One reason for this complexity is likely due to the highly interactive nature of lipid signaling pathways that recruit different signaling pathways and mechanisms of action. Indeed, endocannabinoids are known to interact with the cyclooxygenase enzyme, inhibit the transcription of genes involved in metastatic processes, induce cell cycle arrest, activate the formation of reactive oxygen species, and ensure the integrity of rafts/caveolae necessary for anti-proliferative properties. However, other mechanisms are also likely to be involved and interact with the endocannabinoid system in ways yet to be discovered.[15].

Despite the need for further in vitro and in vivo studies, the literature is almost unanimous in suggesting that cannabinoids and endocannabinoids reduce cancer progression in both preclinical in vivo and in vitro studies.[15].

Furthermore, because cannabinoids attenuate chemotherapy-induced neuropathy through CB1 and CB2-dependent mechanisms (Rahn and Hohmann, 2009 for review), there remains the possibility that cannabinoids, in combination with chemotherapy, may enhance both the anti-tumor actions of chemotherapy and mitigate unwanted iatrogenic side effects (e.g., vomiting, neuropathy).[15].

Further fundamental research on the anticancer properties of cannabinoids, as well as clinical trials evaluating the effectiveness of cannabinoids in cancer, are needed before the use of cannabinoids can be established and accepted as an effective complement to cancer treatment [15].

Cannabis in Epilepsy

According to a systematic review of controlled evidence published in the Journal of Neurology, Neurosurgery & Psychiatry in 2018, it was found that the available evidence on the safety and efficacy of cannabinoids as adjunctive treatment to conventional antiepileptic drugs in the treatment of drug-resistant epilepsy . In many cases, there was qualitative evidence that cannabinoids reduce seizure frequency in some patients, improve other aspects of patients' quality of life, and are generally well-tolerated with mild to moderate adverse effects. There was also evidence that studies with a high risk of bias reported higher proportions of participants reporting seizure reduction and lower proportions reporting adverse effects. In randomized controlled trials and most non-randomized controlled trials, cannabinoids were used as adjunctive treatment rather than a standalone intervention [16].

Additionally, according to the systematic review "Medical cannabis for the treatment of chronic pain and other disorders: misconceptions and facts," studies on the efficacy of cannabinoids in adults with epilepsy have yielded mixed results.[16].

However, a recent study on patients from a tertiary epilepsy clinic showed that cannabis does not affect the frequency or severity of seizures. Although many studies have been published regarding the effects of cannabinoid use on seizures in adults, most of these studies have not been placebo-controlled and have been largely anecdotal.[16].

Most studies have not been placebo-controlled and have been largely anecdotal, highlighting the need for controlled randomized trials. Only 4 placebo-controlled studies have examined the efficacy of cannabinoids in epilepsy, but they had small sample sizes and methodological difficulties. Cannabinoids have shown improvement in epilepsy symptoms, but the data were insufficient to draw firm conclusions [11].

The use of cannabis in epilepsy is the subject of numerous studies, although their quality varies, necessitating the need to strengthen this field. The lack of formal data complicates the response to patients and physicians, and research results are indeed highly variable.[15].

Cannabis in Psychiatry

- Post-Traumatic Stress Disorder (PTSD)

THC, CBD, and THC-CBD combinations have been reported to improve sleep quality and duration as an additional benefit in patients primarily treated for conditions such as pain, Parkinson's disease, sleep apnea, anxiety disorders, and post-traumatic stress disorder (PTSD) (Johnson et al., 2013; Chagas et al., 2014; Farabi, Prasad, Quinn, & Carley, 2014; Roitman, Mechoulam, Cooper-Kazaz, & Shalev, 2014; Blessing, Goddard, Mauro, & Orellana, 2015), although most studies have been of short duration.

A recent study conducted on 11 adults with PTSD evaluated patients over 8 weeks of CBD treatment (capsule or spray; average dose of 49 mg/week) (Elms L, Shannon S, Hughes S, Lewis N. et al., 2019). The results revealed a 28% reduction in PTSD symptoms, but no statistical analysis of the data was performed, so definitive conclusions cannot be drawn. Another retrospective study analyzing PTSD symptoms collected during 80 psychiatric evaluations of patients enrolled in the New Mexico medical cannabis program between 2009 and 2011 (Greer GR, Grob CS, Halberstadt AL, 2014) showed more favorable results, with data indicating a reduction of over 75% in clinic-rated PTSD symptoms.

However, the prevailing opinion among psychiatrists is that there is not yet sufficient evidence to support cannabis as an appropriate treatment for PTSD, as it is a complex condition in which a variety of different mechanisms could be involved (Papini, Sullivan, Hien, Shvil, & Neria, 2015).

- Depression

A potential application for modulation of the endocannabinoid system and the 5HT1A receptor has been used to obtain an antidepressant effect (Russo EB. Br J Pharmacol. 2011).

Three studies evaluating orally administered nabiximols for other conditions (multiple sclerosis) found no significant effect on the secondary outcome of depression (Allsop DJ, Copeland J. et all 2014, Podda G, Constantinescu CS. et all 2012, Trigo JM, Soliman A. et all 2018).

Interestingly, a study of cancer patients using nabiximols showed that a significant reduction in mood occurred in those using a high dose (11-16 sprays per day) compared to placebo (Portenoy RK, Ganae-Motan ED. at all 2012). In addition, a cross-sectional survey of use patterns and perceived efficacy suggested that of over 1429 participants identified as medical cannabis users over 50% reported using medical cannabis specifically for depression (Sexton M, Cuttler C, Finnell JS. at all 2016) .

- Schizophrenia

Consistent evidence has shown a relationship between schizophrenia and cannabis use (D'Souza DC, Sewell RA. et all 2009). A 2016 meta-analysis showed that cannabis dependence is associated with an increased risk of psychosis, especially in adolescents.

However, it is important to mention that schizophrenia is the result of various gene-environment interactions and several key genes have been implicated as being able to modulate the risk of developing schizophrenia after early cannabis use: the CNR1, COMT, AKT1 and DRD2 genes (Kraan T, Velthorst E. et all 2016).

As far as current research is concerned, apart from a study conducted by Zuardi, Morais in 1995, which showed that 1,500 mg of CBD administered for 26 days was beneficial for treatment-resistant schizophrenia, three clinical studies exist to date. A study by Leweke, Piomelli (Leweke FM, Piomelli D et all 2012) tested, in a double-blind trial, 600 to 800 mg/day of oral CBD versus the antipsychotic amisulpride over 4 weeks in 42 patients. While both treatments were safe and led to significant non-differential clinical improvements, the CBD group experienced fewer side effects.

Another double-blind, parallel-group study involving 88 schizophrenic patients who received either oral CBD (1000mg/day) or placebo as an adjunct to existing antipsychotic treatment found that after 6 weeks of treatment the CBD group had lower levels of psychotic symptoms (McGuire P, Robson P, Cubala WJ. et all 2018).

- Bipolar disorder

To date, no clinical trials have evaluated CBD for the treatment of bipolar disorder, although there is a potential role for the endocannabinoid system in this disorder, as noted above. Early case reports argue that this approach may not be beneficial however (Zuardi A, Crippa J. et all 2010). Two patients diagnosed with bipolar disorder type I according to the DSM-IV and presenting depressive symptoms received CBD-based adjunctive treatment (1200 mg per day) after

having received a placebo for an initial period of five days. An improvement in symptoms was shown on olanzapine plus CBD, no further improvement was shown on CBD monotherapy and no side effects were reported.

3.1.3. Contraindications

Five types of patients are generally considered by doctors to be unsuitable for medication with pure cannabinoids that act viaU CB1 or CB2:

Pregnant women : If cannabis is smoked during pregnancy or if pure cannabinoids are taken orally, whether for medical reasons or not, they cross the placenta and can have harmful effects on the foetus (Porath-Waller, 2015). If the mother uses cannabis after giving birth, cannabis is secreted in breast milk and can harm the newborn (Behnke and Smith, 2013; Metz and Stickrath, 2015).

Children and adolescents: Cannabis can have serious adverse effects on various aspects of mental and emotional development, depending on the age of onset, duration and intensity of use (George and Vaccarino, 2015).

An exception could be made for children with certain forms of severe childhood epilepsy that do not respond to conventional anti-epileptics, but do respond to CBD.

People with a history of problematic substance use, whether alcohol, prescription drugs or illicit drugs.

People with a personal or family history of psychosis: They are at greater risk of developing acute psychosis through the use of cannabis or THC-type cannabinoids.

People with pre-existing heart and coronary artery disease.

Tolerance

The development of tolerance is low and depends on the dosage and duration of consumption.

At low doses and for certain therapeutic indications (muscle relaxation, appetite stimulation), tolerance develops very little, even after several months of treatment [17].

Chronic cannabism" therefore encompasses the signs encountered during acute cannabinoid intoxication, with a lesser intensity due to pharmacodynamic tolerance.

For example, the tachycardia recorded following a new intake of cannabis is less severe than during the course of an acute intoxication [18].

Addiction

The risk of dependence on cannabis is low, even after prolonged use.

However, sleep disturbances, excessive sweating and nervous irritability may occur for a few days. But mental dependence is possible in people with fragile minds. When cannabis is used for medical purposes, the risk of psychological dependence is also very low [19].

3.2. Regulatory aspects worldwide

At international level, cannabis is one of the drugs covered by the UN narcotics control regime, which is based on three treaties:

- The 1961 Single Convention on Narcotic Drugs.
- The 1971 Convention on Psychotropic Substances.
- The 1988 United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

Long classified in schedules I and IV of narcotic drugs (schedule IV includes substances with a high potential for abuse and addiction and no therapeutic value), cannabis was removed from the latter in December 2022, a symbolic decision by the UN recognising the plant's therapeutic potential [20].

3.2.1. In the United States

The first US state to legalise cannabis for strictly medical use was California, with the adoption of Proposition 215 or, more precisely, the "Compassionate Use Act" in 1996, which authorised eligible patients to use medical cannabis despite the absence of safety and efficacy tests. Today, medical use of the plant is legalised in 37 states (out of a total of 50). [21]

However, there are major legislative differences between these states: in some, the legislation in force is extremely restrictive, while in others it is much less so[19]. Broadly speaking, the states can be divided into the following three categories:

States where only products containing CBD are legal: for example Epidolex ®, a medicine approved by the FDA for the treatment of epileptic disorders, on prescription [22].

States where medical cannabis is legal: the patients concerned are given an identity card proving that the bearer is using cannabis for medical purposes, and a list of specific conditions and illnesses is defined at state level. Cannabis can be supplied to patients by approved dispensaries known as "Cannabis Buyers Clubs", or grown at home by the patient.

States where cannabis is legal: since 2012, a growing number of states have allowed any adult to buy marijuana without a medical cannabis card. However, for therapeutic uses, it is recommended that you obtain a medical cannabis card and take your doctor's advice, particularly to avoid any drug interactions[23, 24].

However, medical cannabis remains illegal at federal level. It is classified as a Category I drug (with a high potential for abuse), and has no recognised medical use. The first federal reform concerning research into medical cannabis will be introduced in the coming months. Last December saw the historic signing of the medical cannabis bill by Joe Biden [25,26, 27].

3.2.2. In Canada

In Canada, cannabis has been permitted for medical purposes since 2001 following the Ontario Court of Appeal's decision in R. v. Parker in 2000 that the prohibition of cannabis for medical purposes violated the right to equality under the Canadian Constitution. Regulation has since evolved with, in particular, the Cannabis Act and the Cannabis Regulations, which came into force on 17 October 2018 and are now the main legislative instruments governing cannabis in Canada. They repeal the former legislation governing cannabis for medical purposes as well as the Access to Cannabis for Medical Purposes Regulations (ACMPR).

Since then, there have been four ways to obtain cannabis (dried leaves, oil) for medical purposes:

- From a producer approved by Health Canada.
- By producing your own cannabis after registering with the Ministry of Health.
- By appointing a person to produce it on the basis of a medical document.
- For adults, by purchasing it at retail outlets or via authorised online sales platforms.
- Generally speaking, cannabis can be used for any symptom.

As far as industrial products are concerned, Sativex®, indicated for the treatment of spasticity in multiple sclerosis, is available for sale. Dronabinolle (Marinol ®) has been withdrawn from the Canadian market voluntarily by the manufacturer[29] [30].

3.2.3. In Europe

In Europe, the process has accelerated and many countries have or are in the process of legalising medical cannabis. There are as many situations as there are States. The Netherlands pioneered the process in 2003. It has since been followed by more than twenty of the 27 countries, including Switzerland, Belgium, Italy and Germany. The most common initial approach has been to use some form of special access regime, generally creating a system of medical approval and supervision, limiting medical use to a restricted set of conditions and often restricting the cannabis-based preparations that patients can use[31, 32].

The Netherlands

In the Netherlands, all doctors can prescribe medical cannabis. Pharmacies can also produce extracts from plant material produced by the Office of Medical Cannabis (OMC) under the supervision of the Ministry of Health, Welfare and Sport. These are generally oil extracts to be taken orally or placed under the tongue. Certain types of inflorescence are

available for this purpose: the concentration of active molecules and granulation properties may vary. Inflorescences can also be taken as a decoction or inhaled through vaporisers. Cannabis is indicated for treating the symptoms of pathologies including, but not limited to, multiple sclerosis, HIV, cancer, pain and Tourette's syndrome, refractory glaucoma, epilepsy and epileptic syndromes (even in children)[32,33].

France

In France, three cannabis-based medicines are authorised. Sativex® has had permanent authorisation since 2014 but is still not available in France. It is, however, available in neighbouring countries. Marinol® and Epiolex® are covered by temporary use authorisations (ATU), but the procedure for patient access remains highly complex. Since 2021, therapeutic cannabis has been tested in a number of very specific indications, including pain that is refractory to available therapies; certain forms of severe, drug-resistant epilepsy; supportive care in oncology; palliative situations; and painful spasticity in multiple sclerosis. Ultimately, depending on the results of the study, the dispensing of medical cannabis will be supervised by pharmacists, initially in hospital pharmacies and then in community pharmacies. Under no circumstances will it be intended for smoking[32] [34].

3.2.4. In Asia

Few countries are taking an interest in the still fairly taboo issue of cannabis. Thailand has recently taken the path of legalisation through the 2019 Narcotics Act. Government research organisations, the medical profession and patients are granted licences to consume, possess, use for research purposes or cultivate and market cannabis in accordance with specific guidelines. China recently decided to legalise medical cannabis and CBD, authorising 1,600 hectares for cultivation, but still does not have a medical programme in place[35] [36].

3.2.5. In Africa

In Africa, the number of countries authorising the cultivation of cannabis for medical purposes continues to grow. Most of the countries concerned authorise cultivation for export purposes only, but others allow cannabis to be used for medical purposes on their territory [37,38].

Algeria

The cultivation, trade and possession of cannabis and cannabis products are prohibited in Algeria, except for medical and scientific purposes, subject to authorisation by the Minister of Health. However, the country does not currently have any medical cannabis programmes (law 04-18/ implementing decree 07-228)[37].

Morocco

In Morocco, Law 13-21, governing the legal use of cannabis for medical, cosmetic or industrial purposes, came into force at the end of July 2021, covering several aspects of the forthcoming transition, including the areas that may be cultivated, the conditions for granting authorisations for cultivation, and the type of beneficiaries affected by this reform. The country has also set up a regulatory body, the National Agency for the Regulation of Cannabis-Related Activities, whose mission is to control all stages of the production chain, from the import of seeds and the certification of plants to the marketing of products[38].

3.2.6. Other

Several South American countries have or are in the process of legalising medical cannabis. Colombia, for example, authorises the import and export of cannabis, Peru only authorises it for certain illnesses, Paraguay authorises the import of cannabis oil and self-cultivation for medical use, Argentina authorises the import and medical use of cannabis oil, Brazil only authorises medicines and cannabis-derived products with a THC concentration not exceeding 0.2%. [39,40,41].

In Australia, several medicines are authorised, including Sativex® and Epidiolex®. Cannabis plant-based products are subject to authorisation by the Therapeutic Goods Administration, the Australian equivalent of the FDA[42].

4. Conclusion

The use of cannabis for medical purposes thanks to cannabinoids is a form of medical therapy for treating various illnesses or relieving symptoms. Cannabinoids can be administered in a variety of ways, including orally, sublingually or topically, as well as by smoking, inhaling, mixing with food or processing into tea, or in the form of natural extracts.

In some countries, medicinal-grade cannabis has been legalised for use by patients suffering from chronic illnesses. For example, Canada and the Netherlands both have government-run programmes that provide quality-controlled herbal cannabis. In the United States, 36 states and Washington D.C. have passed laws authorising the medical use of cannabis. Other countries are even making therapeutic cannabis a major economic issue.

Compliance with ethical standards

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Disclosure of conflict of interest

The author and declare that he has no conflicts of interest inconnection with this document.

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