



Review

An Insight into the Use of Cannabis in Medical and Veterinary Dermatological Applications and its Legal Regulation

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Abstract:

Cannabis contains more than 140 cannabinoid compounds, of which cannabidiol and tetrahydrocannabinol are the most exposed ones, as they have the potential for numerous applications in various fields of health and medicine. Many scientific findings and numerous clinical studies over the last decade report results related to pain relief, treatment of chronic diseases and certain neurological disorders in human medicine. In line with the growing trend of research and application in human medicine, the research and application potential in veterinary medicine is also increasing. Of the biologically active molecules contained in the plant, cannabidiol has attracted the most interest. The cultivation of cannabis for medical and pharmaceutical purposes requires, among other things, compliance with legal regulations. An analysis of the legal acts regulating the use for medical and pharmaceutical purposes shows that the current regulation at state level is complex and should be amended.

Keywords: Cannabis, Cannabinoids, Human medicine, Veterinary medicine, Inflammation, Legal Regulation



1. Introduction

Cannabis sativa stands as a botanical enigma deeply ingrained in human history, weaving a rich tapestry across ancient cultures. From being a crucial agricultural crop and industrial raw material to its multifaceted roles in contemporary society – medical, nutritional, and industrial cannabis has evolved as a subject of intense scientific inquiry. Its origins date back to more than a millennium BC and cannabis played a central role in agriculture until the late 19th century (Zuardi, 2006). The year 2019 marked an important turning point with the European Parliament's resolution supporting the medicinal use of cannabis (Pečan et al., 2021). This has driven efforts towards decriminalisation in the European Union, the promotion of research and the integration of medicinal cannabis in EU countries. At the same time, the Commission on Narcotic drugs recognised cannabis, particularly Δ^9 -tetrahydrocannabinol (Δ^9 -THC, THC) (Figure 1 (b)), as a substance that primarily causes no harm, which shaped the international monitoring framework (Pečan et al., 2021; Štukelj et al., 2019).

Cannabis, which botanically belongs to the Cannabaceae family, is a dioecious, flowering plant characterised by remarkable adaptability. The leaves are palmately compound or toothed with toothed leaflets. The phenotypic expression of the plant is strongly influenced by environmental factors, which makes it an interesting subject for detailed botanical studies (Amaducci et al., 2008).

Modern scientific research has identified over 420 compounds in cannabis (Atakan, 2012). Trichomes, specialised secretory glands concentrated in the female inflorescences, contain cannabinoids, terpenes and flavonoids, fundamental components of the secondary metabolism of cannabis (Tanney et al., 2021). Cannabinoids, more than 90 different substances, have a binding affinity to cannabinoid receptors and thus trigger a spectrum of physiological effects (Andre et al., 2016).

As the primary psychoactive component, THC plays a central role in the pharmacological profile of cannabis (Bridgeman and Abazia, 2017). Classified as a narcotic, THC acts as a partial agonist at the cannabinoid receptors CB1 and CB2, particularly in the central nervous system and the immune system, and thus unfolds its psychotropic effect (Pertwee 2008). THC is approved for medical applications and plays an important role in drugs such as Marinol®, Cesamet™ and Sativex® (Tavčar Benković et al., 2019).

Cannabidiol (CBD) (Figure 1 (a)) was reported in 1940 (Burstein, 2015) and has developed into an important phytocannabinoid with a wide range of applications. CBD has analgesic, anti-inflammatory, antineoplastic and chemopreventive effects and differs from THC in that it is not psychoactive (Martínez et al., 2020). Its complex mechanisms include stimulation of endoplasmic reticulum stress, inhibition of AKT/*m*TOR signalling and activation of autophagy, which offers diverse therapeutic potential (Pertwee, 2006).

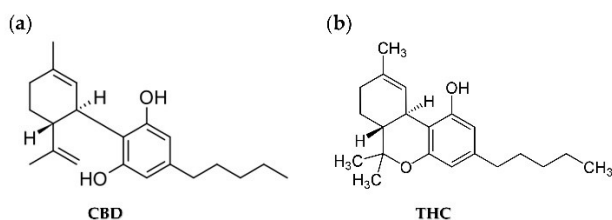


Figure 1. Structures of (a) cannabidiol (CBD) and (b) Δ^9 -tetrahydrocannabinol (THC).

Cannabis and its derivatives have made a name for themselves in the pharmaceutical industry, particularly for dermatological problems (Martins et al., 2022). Cannabinoids such as CBD have anti-inflammatory and analgesic properties, making them promising candidates for the treatment of conditions such as psoriasis and eczema (Baswan et al., 2020). Pharmaceutical formulations containing cannabis extracts are being investigated for their potential for topical treatments that provide targeted relief (Baswan et al., 2020).

In veterinary medicine, cannabis and its derivatives are currently being carefully investigated for their potential therapeutic benefits. Studies suggest that cannabinoids may



be useful in the treatment of certain conditions such as osteoarthritis and epilepsy in animals (Di Salvo et al., 2023). This emerging field offers the possibility of tailored veterinary treatment, taking into account species-specific responses and dosing considerations (Gupta et al., 2019).

Cannabis, deeply rooted in antiquity, is evolving into a complex botanical entity with profound implications for historical understanding and contemporary applications. Research into the complex botanical and pharmacological dimensions of cannabinoids such as THC and CBD forms the basis for careful scientific investigation. The dynamic legal landscape and increasing applications underscore the need for rigorous research that places cannabis at the forefront of scientific exploration, offering potential advances in human and veterinary medicine and opening new dimensions for specialized pharmaceutical formulations (Pečan et al., 2023).

2. Cannabis extracts and cannabinoids for the treatment of skin diseases in human medicine

The long history of the use of cannabis for medicinal and recreational purposes has also led to its use for various skin applications. Cannabis extracts have been investigated as a potential remedy for skin problems and disorders (Shao et al., 2023). The therapeutic potential of the cannabinoid CBD has been particularly researched and studied as it is abundant in the cannabis plant and has a relatively favourable legal status compared to THC. Recently, extensive review articles have been published on the therapeutic potential of phytocannabinoids, particularly cannabidiol, focusing on its effect on skin health, disease (Baswan et al., 2020; Martins et al., 2022) and delivery mechanisms (Filipiuc et al., 2023). Natural cannabinoids, including CBD, have been shown to have a positive effect in the treatment of many skin diseases (Baswan et al., 2020). Their effect is mainly due to the fact that the endocannabinoid system (ECS) has an important regulatory function in the skin (Baswan et al., 2020) and therefore effective preparations can be used when applied topically. Cannabinoids are an interesting field of research in dermatology due to their anti-inflammatory, antipruritic and antinociceptive properties (Shalaby et al., 2018).

2.1. Atopic dermatitis and eczema

Atopic dermatitis (AD) and eczema are chronic conditions that lead to inflammation, redness and irritated skin. Many factors can lead to atopic dermatitis, such as a damaged skin barrier, an unwanted immune response and an imbalance in the microbiome (Dimitriu et al., 2019). The anti-inflammatory effect of CBD was investigated in an experimental model (Petrosino et al., 2018). This study has shown that CBD inhibits the production of the chemokine MCP-2 and several other proinflammatory cytokines in poly-(I:C)-stimulated keratinocytes more effectively than other non-psychotropic phytocannabinoids tested. Clinical studies have yet to be conducted. Several studies have suggested using the skin ECS as a potential treatment for AD (Mounessa et al., 2017). Studies in mice showed that activation of cannabinoid 1 receptor (CB1R) in skin cells has a positive effect on epidermal barrier function and reduces a Th2-type inflammatory response (Gaffal et al., 2014; Kim et al., 2015).

In an earlier study, the consumption of cannabis seed oil was compared with olive oil (Callaway et al., 2005); in a 20-week randomized, single-blind crossover study with AD patients, the treatment was carried out with a daily intake of 30 mL cannabis seed oil or olive oil (Callaway et al., 2005). The intake of cannabis seed oil led to significant changes in plasma fatty acid profiles and a reduction in skin dryness, skin irritation and itching compared to olive oil. The authors assume that this effect is due to the high proportion of polyunsaturated fatty acids (PUFAs) in cannabis seed oil.

An unbalanced skin microbiome could also have an important influence on the severity of dermatitis; the studies suggest that the main antimicrobial effects of cannabis come from its essential oil (Mediavilla et al., 1997), *i. e.* the volatile component of cannabis. Its main components are terpenes such as myrcene, α -pinene, β -caryophyllene and others. The antimicrobial effect has been proven against *S. aureus* (Zengin et al., 2018).



2.2. Acne and seborrhea

Acne and seborrhea are well-known skin diseases characterized by irregularly increased sebum production by the sebaceous glands (SC). Acne as a skin disease occurs when the hair follicles become clogged with oil and dead skin cells. Sebum overproduction, inflammation and altered sebocyte proliferation are the most important factors in the appearance of acne on the skin. The endogenous endocannabinoids (ECBs) are involved in the maintenance of homeostatic sebum production in the human sebaceous glands (Dobrosi et al., 2019). Several studies confirm that CBD could play an important role in the treatment of acne due to its effect on acne-related factors (Oláh et al., 2014). An important study was conducted to test the anti-inflammatory effect of CBD on human sebocytes (Oláh A et al., 2014). The study suggests that CBD is not limited to a direct ECS interaction, but has a more generalized effect. More importantly, CBD not only acts as a lipid-lowering agent but also stabilizes lipid imbalance by normalizing lipogenesis (Jin and Lee, 2018). In addition, CBD has been shown to reduce overall cell proliferation at some relevant doses (Oláh et al., 2014). The same research group has tested the anti-inflammatory potential of CBD and demonstrated its effect (Oláh et al., 2014). The anti-inflammatory effect was attributed to the A2a adenosine receptor-dependent upregulation of Tribbles homolog 3 (TRIB3) and inhibition of the NF- κ B signaling pathway. The study concludes that CBD could be a promising therapeutic agent for the treatment of acne due to its combined lipostatic, antiproliferative and anti-inflammatory effects (Oláh et al., 2014).

An unbalanced skin microbiome can contribute to the occurrence of acne, especially the overgrowth of *C. acne* (Platsidaki and Dessinioti, 2018). The study (Jin and Lee, 2018) using cannabis seed hexane extract showed that it has an antimicrobial effect on *C. acnes*. It also induced inflammation and lipogenesis in sebocytes. Cannabis seeds have a minimal CBD content (Callaway, 2004), so we cannot draw parallels regarding their effect on the acne skin microbiome. More promising results could be expected from the use of cannabis essential oil, which mainly contains terpenes (Vuerich et al., 2019). These have been shown to have an antimicrobial effect against *C. acnes* (Raman et al., 1995).

2.3. Psoriasis

Psoriasis is a chronic, inflammatory autoimmune disease of the skin in which the immune system becomes overactive and causes hyperproliferation of skin cells, followed by skin changes known as psoriatic plaques and inflammation (Michalek et al., 2019). Recent research (Sangiovanni et al., 2019) has shown that CBD and cannabis extract (*C. sativa*) standardized to 5% CBD (CSE) inhibit TNF- α -induced NF- κ B inhibitory effects in HaCaT cells. NF- κ B is a family of transcription factor protein complexes that regulate DNA transcription, cytokine production and cell survival (Wu et al., 2003). It plays an important role in inflammatory skin diseases, usually associated with psoriasis (Sangiovanni et al., 2019). CSE treatment reduced all 26 genes associated with inflammation, while CBD alone reduced only 15 genes (Sangiovanni et al., 2019). This suggests that a broad range of cannabinoids could achieve better results than CBD alone. The use of phytocannabinoids for the treatment of psoriasis should be used with caution. A study on the treatment of psoriasis with CBD (Casares et al., 2020) has also shown that it has proliferative effects on keratins 16 and 17. This could lead to additional complications for psoriasis patients.

3. Cannabis in veterinary dermatology

Dermatologic diseases are the main reason for consultations in general veterinary small animal clinics after preventive health care (Hill et al., 2006). Skin diseases encompass a variety of different conditions, but in most cases an inflammatory response triggered by an infectious, parasitic or immunologic stimulus is the main mechanism behind the pathologic process (Scott & Paradis, 1990). Therefore, pruritus is the most commonly observed sign, especially in dogs (Khoshnegah et al., 2013). In cats, swelling of the skin appears to be the predominant clinical presentation (Hill et al., 2006). Bacterial skin infections are also common in dogs, with *S. pseudintermedius* being the main cause in most cases (Bourguignon et al., 2013). Consequently, the most commonly prescribed drugs for the treatment of skin diseases in small animals are systemic antibiotics and glucocorticoids



(Hill et al., 2006). Topical treatments may also be prescribed for localized skin lesions (Mueller et al., 2012). The commercially available formulations used in veterinary medicine are very similar to those used in humans. They are mainly topical creams and ointments with antibacterial or anti-inflammatory agents to heal skin lesions.

The inclusion of novel molecules with anti-inflammatory, immunomodulatory and antimicrobial effects such as cannabinoids (Izzo et al., 2009) could expand the therapeutic arsenal for dermatological diseases.

The endocannabinoid receptors (CB1 and CB2) are expressed in different cell types of the epidermis and dermis of healthy dogs (Campora et al., 2012), cats (Miragliotta et al., 2018) and horses (Kupczyk et al., 2022). CB1 receptors have also been found in the inner root sheath cells of the primary and secondary hair follicles of dogs (Mercati et al., 2012). The ECS appears to play a protective role in inflammatory dermatological conditions, as ECS expression has been reported to be increased in canine atopic dermatitis (Campora et al., 2012) and in cats with hypersensitivity dermatitis (Miragliotta et al., 2018).

Cannabidiol (CBD) and Δ -9-tetrahydrocannabinol (THC) are the best-studied phytocannabinoids in veterinary medicine (De Mendonça Lima et al., 2022). The use of CBD and THC is considered safe for dogs (Vaughn et al., 2020) and cats (Kulpa et al., 2021). CBD is better tolerated than THC, as escalating doses of CBD resulted in mild adverse effects in both dogs and cats (Vaughn et al., 2020; Kulpa et al., 2021). High doses of THC can cause moderate to severe adverse effects in pets, such as lethargy, hypothermia and ataxia (Vaughn et al., 2020; Kulpa et al., 2021). However, THC has a high therapeutic index, as maximum doses of this compound do not cause death in dogs (Beaulieu, 2005).

Pharmacokinetic studies in dogs have shown that the oral bioavailability of CBD is low, ranging from 13 to 19% (Samara et al., 1988). Although other administration methods have also been tested, oral administration is still the preferred route of administration in most pharmacological studies on cannabinoids in veterinary medicine (Corsato Alvarenga et al., 2023). For focal dermatological conditions, cannabinoids can be administered via the transdermal route to maximize skin concentration while allowing absorption into the bloodstream (Bartner et al., 2018; Hannon et al., 2020). To this end, cannabinoids could be formulated as ointments, preferably as native acid derivatives, as acidic forms of CBD and THC have been shown to be better absorbed than their decarboxylated counterparts (Hannon et al., 2020).

In veterinary medicine, the clinical efficacy of CBD has been tested mainly in osteoarthritic pain, epilepsy and behavioural disorders (De Mendonça Lima et al., 2022; Di Salvo et al., 2023). For skin diseases, two studies focused on testing the potential benefits of cannabinoids in atopic dermatitis in dogs (Loewinger et al., 2022; Mogi et al., 2022). In both studies, cannabinoids were able to reduce itching, although no clinical differences in skin lesions were observed compared to the control groups (placebo) (Loewinger et al., 2022).

Infectious diseases of the skin could be another potential clinical target for cannabinoids. Infections on the skin surface of animals can not only prolong the patient's recovery time, but also spread to other parts of the body, invade the bloodstream and migrate to the internal organs, which can prove fatal if left untreated for too long. Amoxicillin and cefalexin are the most commonly prescribed systemic drugs for skin infections in veterinary dermatology (Hill et al., 2006). Cannabis derivatives exert antimicrobial properties on a broad spectrum of pathogenic bacteria (Schofs et al., 2021). Cannabinoids could act against *S. pseudintermedius*, the main cause of skin infections in dogs (Bourguignon et al., 2013; Aiensaard et al., 2022), but also against skin infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), a pathogen important for both public health and animal health (Haag et al., 2019; Pečan et al., 2023). These antimicrobial effects of cannabinoids could be further explored in clinical trials in veterinary medicine to test *in vivo* efficacy against skin infections.

Laboratory animal models are not always of translational use, as in many cases they have not been able to predict clinical efficacy and toxicity in humans (Ritter et al., 2020; Marshall et al., 2023). As part of a "One Health" approach and utilising naturally occurring diseases in dogs and cats, cannabinoids can therefore be used as a potentially useful tool in both veterinary and human medicine.



4. Legal regulation of medical cannabis in Slovenia

The history of cannabis regulation is marked by an evolving understanding and shifting legal frameworks. Initially used for medicinal and recreational purposes in various cultures, cannabis' perception underwent a significant transformation in the 20th century. This period saw the international community, through agreements like the 1961 Single Convention on Narcotic Drugs, categorize cannabis as a controlled substance, significantly restricting its use globally (United Nations, 1961). However, recent decades have witnessed a re-evaluation, especially in the context of medical cannabis. This shift has been propelled by a growing body of scientific research that underscores the therapeutic potential of cannabis, particularly in managing chronic pain and other medical conditions (Whiting et al., 2015). Consequently, many countries have begun to adapt their legal frameworks, creating distinct regulations for medicinal and recreational cannabis use. Today's regulatory landscape of cannabis is a complex amalgamation of medical research, legal policies, and evolving societal attitudes (Hall & Lynskey, 2016). This article focuses specifically on cannabis as a plant and does not address cannabinoids that are synthesized independently of the cultivation of the plant.

4.1. Cannabis as an illegal drug

Zakon o proizvodnji in prometu s prepovedanimi drogami (Production of and trade in illicit drugs act: **Law 1**) specifies the conditions under which the production and trafficking of illegal drugs, as well as the possession of illegal drugs, are permitted. The law requires the Government of the Republic of Slovenia, upon the proposal of the minister responsible for health, to adopt the classification of illegal drugs into the following three groups:

- *Group I*: Plants and substances that are extremely dangerous for human health due to the severe consequences that can result from their abuse and are not used in medicine;
- *Group II*: Plants and substances that are extremely dangerous due to the severe consequences that can result from their abuse but can be used in medicine;
- *Group III*: Plants and substances that are moderately dangerous due to the consequences that can result from their abuse and can be used in medicine.

According to the currently valid *Uredba o razvrstitvi prepovedanih drog* (Decree on the classification of illicit drugs: **Decree 1**), cannabis, or scientifically *Cannabis sativa* L., as a plant, or its resin and extracts are classified in Group II. Cannabis is thus an illegal drug according to Slovenian law.

4.2. Under the gaze of Article 186: The regulation of cannabis in Slovenia

In the context of illegal drugs, the Slovenian *Kazenski zakonik* (Criminal code: **Law 2**), specifically Article 186, addresses the unauthorized production, processing, sale, offer for sale, or acquisition for the purpose of sale or distribution of illegal drugs. This legal framework is crucial for understanding the criminal implications of cannabis-related activities in Slovenia.

Article 186 states that anyone who unjustifiably produces, processes, sells, offers for sale, purchases, stores, or transports drugs, or facilitates their sale or purchase, is subject to legal penalties. This article is applied in situations involving cannabis when these activities are conducted without proper authorization or in violation of existing regulations.

The application of Article 186 to cannabis-related activities underscores the seriousness with which the Slovenian legal system treats the control of illegal drugs. This includes cannabis, which, despite its varying legal status in different jurisdictions (including Slovenian), remains under strict regulation in Slovenia. The law aims to prevent unregulated and potentially dangerous drug trafficking, ensuring public health and safety by controlling the production and distribution of such substances.

4.3. Exclusion of illegality

Although in the case of the specific criminal act under Article 186, we could even talk about the non-fulfillment of the statutory characteristics, as it emphasizes unauthorized production, sale, etc., due to systematic correctness and the possibility of future



amendments to the text, the author adopts a position that will always exist regardless of the text of the criminal code, as it originates from the theory of criminal law.

To understand how exactly legal acts then permit its use for medical purposes, it is necessary to briefly explain the theory of a criminal offense. For an act to be considered criminal, an individual's conduct must meet specific conditions, which are described in the *Kazenski zakonik (Law 2)*.

When an individual does this, it is necessary to examine whether they acted in circumstances that, despite meeting all the characteristics, make their conduct completely in accordance with the law. This is called the exclusion of illegality. One way to exclude illegality is through exclusion by another law, meaning another law, not the criminal code, permits a certain behaviour that would otherwise be criminal according to the criminal code.

4.4. Regulation of registered cannabinoid medicines in Slovenia

Under the Slovenian Law on the *Zakon o proizvodnji in prometu s prepovedanimi drogami* (Production of and trade in illicit drugs act: *Law 1*), registered medicines that contain cannabis and its naturally derived active substances are not considered illegal drugs, provided they are obtained and handled legally. Article 6 exempts such substances from being categorized as illegal drugs when they are used in accordance with specific regulations (*Zakon o lekarniški dejavnosti* (Pharmacy practice act: *Law 3*) in *Zakon o zdravilih* (Medicinal products act: *Law 4*). Consequently, these substances are not implicated in the criminal offense described in Article 186 of the Criminal Code, which deals with the unauthorized production and trafficking of illegal drugs. As of the time of research, there are 24 such medicines registered in the central database of drugs, including those that are only authorized for import and not for distribution within Slovenia.

4.5. Supply of cannabis for pharmaceutical production

In the context of importing active substances, the exclusion of illegality operates in a somewhat different manner which will be described in the following paragraphs. This approach is essential in jurisdictions where the use of certain substances is permitted for specific purposes, but production is not and therefore all active substances in Slovenia are imported.

The import of active substances for the manufacture of (magistral) drugs with cannabinoids in Slovenia is governed by a complex legal framework, ensuring that only high-quality and safe ingredients are used. The primary legal documents regulating this area are the *Zakon o zdravilih (Law 3)* specifically Articles 119 to 122, and the *Government rules* (Rules on the manufacture, wholesale distribution and import of active substances and on registers of manufacturers, wholesalers and importers of active substances: *Rules 1*). These laws stipulate that only registered importers, who are either holders of a medicinal product manufacturing license, active substance manufacturers, or wholesalers of active substances, are authorized to import such substances.

In terms of magistral drugs with cannabinoids, Slovenian regulations permit the prescription of isolated or synthetically obtained cannabinoids, standardized cannabis flower extract, and phytocannabinoids in the form of floral and fruit tops of medical cannabis. However, the import of standardized cannabis flower extract and its components requires a demonstrated medical need (JAZMP, 2023).

Furthermore, the import of drugs without marketing authorization in Slovenia is permissible only with a specific import permit. The Agency for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP) issues these permits within 30 days upon receipt of a complete application for drugs necessary for individual emergency treatments, essential or urgently needed medicines, and in extraordinary cases or for reasons of public health protection (JAZMP, 2023). The applicant for these permits must be a holder of a wholesale drug trading license or a manufacturer authorized to import drugs.

In summary, the Slovenian legal framework ensures that the import of active substances for (magistral) drugs with cannabinoids is strictly regulated. Importers must be registered and comply with EU or equivalent production standards. Prescribing and importing



cannabinoid-based drugs are subject to stringent controls, emphasizing the necessity of medical justification and adherence to public health interests.

4.6. Industrial hemp cultivation regulations in Slovenia

In Slovenia, the cultivation of industrial hemp is strictly regulated under the *Pravilnik o pogojih za pridobitev dovoljenja za gojenje konoplje in maka* (Rules on conditions for obtaining a permit for hemp and poppy cultivation: **Rules 2**). This legislation mandates that cultivation is permissible solely for certain varieties that are included in the national "Sortna lista" for 2023. These varieties must be listed within the EU and contain a THC content of less than 0.3%.

To engage in hemp cultivation, farmers are required to satisfy various criteria. These include possessing a minimum land area of 0.1 hectares, which is reduced to 0.01 hectares for organic farmers. Additionally, they must register their cultivation activities, providing comprehensive details about the area of cultivation and its intended use.

These stringent measures ensure that Slovenian hemp cultivation adheres to both national and European Union standards. It's crucial to note that the cultivation of medical cannabis, or cannabis suitable for the production of medicines, is currently not permitted in Slovenia. This distinction is important as the term "medical cannabis" specifically refers to varieties used for medicinal purposes, different from those allowed for industrial cultivation.

5. International Resonance and Comparative Perspective

The significance of medical cannabis in the context of human rights has also already been acknowledged. The European Court of Human Rights (ECHR) in the case of *Thörn v. Sweden (Case 1)* examined whether domestic authorities violated the appellant's right to respect for private life by not exempting him from general criminal liability, which applies to such actions. The case emphasizes the cultivation of cannabis for personal medical use and it underlines the necessity for domestic authorities to consider individual circumstances in criminal prosecutions involving medical cannabis cultivation, balancing public drug regulation interests against individual health needs, considering THC content, distribution risk, medical necessity, and legal available alternatives.

In contrast to Slovenia, some EU countries like Germany and the Czech Republic have more liberal approaches towards medical cannabis. Germany has a regulated medical cannabis program with strict quality control measures and a tightly regulated supply chain to ensure patient safety and product consistency. The regulation also covers the import and manufacturing of medicinal cannabis, with strict licensing requirements (Düwel et al., 2023). The Czech Republic permits medical cannabis use with a prescription and allows individuals to cultivate up to five cannabis plants for personal use. As of 2022, decrees regulate the cultivation and processing of cannabis plants for medical use, setting the rules for proper cultivation practice and licensing for Czech growers. There have been efforts to increase the number of suppliers, enable export, and reduce patient costs. The Czech legal framework involves reimbursement of medical cannabis costs and ongoing developments in the regulation of cultivation and supply (KOPAC, 2023) which can sometimes prove ineffective (Medical cannabis network, 2019).

The benefits of liberal medical cannabis regulation in the EU have been recognized. More EU Member States are viewing the clinical benefits of cannabis and its derivatives favorably. There is a movement towards ensuring fair and equal access to medical cannabis products and establishing a harmonized policy framework at the EU level (Lipnik-Štangelj and Razingger, 2020).

6. Conclusion

Cannabis has been very popular throughout human history due to its versatility, as it can be used in various fields such as the textile, paper, food, furniture and energy industries. It contains more than 140 cannabinoid compounds, of which cannabidiol and tetrahydrocannabinol are the most exposed as they have the potential to treat diseases (Čulić et al., 2021). Numerous scientific findings and clinical studies over the last decade agree that the use of cannabis in medicine has undoubted clinical benefits for many



conditions. The best-known effects of cannabis use are pain relief and treatment of chronic diseases and certain neurological disorders in human medicine (Čulić et al., 2021).

The use of cannabis products by humans is increasing worldwide. In veterinary medicine trend is related to the growing interest of clients and veterinarians in the treatment of animal diseases with these molecules. In general, CBD is of primary interest in veterinary medicine (Temmerman, 2023).

In summarizing Slovenia's approach to cannabis regulation, it is essential to recognize the nuanced interplay between legal rigidity and emerging recognition of cannabis's medicinal value. The journey through Slovenia's legal frameworks, particularly the *Zakon o proizvodnji in prometu s prepovedanimi drogami (Law 1)* and Article 186 of the *Kazenski zakonik (Law 2)*, highlights a cautious yet evolving stance towards cannabis.

A critical aspect yet to be fully explored is the potential for domestic production of medical cannabis. The current legislative framework, while stringent on illicit drug activities, has not fully embraced the cultivation of cannabis for medicinal purposes (Štukelj et al., 2018). Developing a regulatory system that permits controlled cultivation for medical production under strict quality standards could significantly enhance Slovenia's healthcare landscape and contribute to global medicinal cannabis research.

This review of Slovenia's cannabis regulation reveals a nation balancing control with emerging medicinal perspectives. The potential for regulatory reform, accommodating both public safety and medical advancement, looms as a promising horizon. Such a future, where regulation aligns with the scientific and compassionate use of medicinal cannabis, could position Slovenia as a leader in this field, reflecting a commitment to both legal integrity and medical innovation.

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Conflicts of Interest: The authors declare no conflict of interest.

List of regulation documents

1. *Law 1:* Zakon o proizvodnji in prometu s prepovedanimi drogami (Uradni list RS, št. 108/99, 44/00, 2/04 – ZZdrI-A in 47/04 – ZdZPZ)
2. *Law 2:* Kazenski zakonik (Uradni list RS, št. 50/12 – uradno prečiščeno besedilo, 6/16 – popr., 54/15, 38/16, 27/17, 23/20, 91/20, 95/21, 186/21, 105/22 – ZZNŠPP in 16/23)
3. *Law 3:* Zakon o lekarniški dejavnosti (Uradni list RS, št. 85/16, 77/17, 73/19 in 186/21)
4. *Law 4:* Zakon o zdravilih (Uradni list RS, št. 17/14 in 66/19)
5. *Decree 1:* Uredba o razvrstitvi prepovedanih drog (Uradni list RS, št. 69/19, 157/20, 162/21, 8/23 in 113/23)
6. *Rules 1:* Pravilnik o proizvodnji, prometu na debelo in uvozu učinkovin ter registrih proizvajalcev učinkovin, veletrgovcev z učinkovinami in uvoznikov učinkovin (Uradni list RS, št. 79/16)
7. *Rules 2:* Pravilnik o pogojih za pridobitev dovoljenja za gojenje konoplje in maka (Uradni list RS, št. 40/11, 36/15, 33/18 in 61/23)
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